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Upper Gastrointestinal Intraabdominal Anastomotic Leak:

Definition, Diagnostic, Management And Prevention

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INTRAABDOMINAL ANASTOMOTIC LEAK AFTER UPPER GASTRO-INTESTINAL SURGERY:

DEFINITION, DIAGNOSIS, MANAGEMENT AND PREVENTION

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A mi madre, Sofía.
Porque sé que allí donde tu estés,
estás disfrutando ver a tus hijas realizarse.

A mi padre, Pedro.
Porque es la fuerza más
inquebrantable que jamás haya visto.

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The best teachers are those who show you where to look, but don´t tell you what to see. *(Alexandra K. Trenfor)*

The scientific man does not aim at an immediate result. He does not expect that his advanced ideas will be readily taken up. His work is like that of the planter –for the future. His duty is to lay the foundation for those who are to come, and point out the way. He lives and labors and hopes with the poet who says:
(Nicola Tesla)

Un país que desprecia la verdad está condenado a la decadencia. *(Harry G. Frankfurt)*

Abstract

The augmenting number of upper gastrointestinal (UGI) procedures, specially due to bariatric surgery, entails an expected increase in the absolute number of surgical complications. Among the most devastating complications is that of a postsurgical leak, increasing morbidity and mortality thus affecting long-term survival rate and treatment's cost. Consequently nowadays we think it should be considered like a real public health problem. Incidence and risk factors are well described in literature. Surprisingly, a definition for this entity nor a management algorithm has not been described yet.

Between 2003 and 2013, 1.856 patients underwent an UGI operation in our center: 121 gastrectomies (total: 58 subtotal: 63); 1.654 gastric bypass; and 81 sleeve gastectomies. 15 (0,08%) patients with confirmed intraabdominal post-surgical leak were reported (10 acute; 5 chronic). Diagnosis methods, management and complications were analized.

Intraabdominal anastomotic leak (IAAL) has been defined in our study as a disruption of esophagojejunal, gastro-jejunal or jejuno-jejunal anastomosis, as well as on the staple line and paraanastomotic abscesses seen on radiological images.

Early diagnosis was possible due to high index suspicion. Identification of patients with severe sepsis or septic shock was provided by SIRS classification. A CT scan with oral and/or intravenous contrast, stablished evidence of leak in 13 patients. Endoscopy verified radiological findings and assessed severity in 9 patients. In 5 cases it was performed before surgery. No differences in rates in reoperation, leakage and postsurgical complications were described in this group. Imminent exploratory laparoscopy was performed in 2 hemodynamic unstable patients.

Treatment was established promptly combining endoscopical, surgical and/or radiological techniques. Management options were determined by hemodynamic conditions of the patient and the characteristics of leakage to assure enteral nutrition as soon as possible. Conservative management was carried out in 4 patients, healing 3 of them. 11 patients submitted surgical treatment (8 laparoscopies; 1 urgent laparotomy; 2 elective surgeries). Stent was deployed in 8 patients (sealing rate: 62,5%).

Abstract

Life-threatening complications requiring ICU management (Clavien-Dindo IV) (33.3%) were more frequent in patients with surgical management. One (6,6%) patient died. Patients with conservative management had short intensive care course (10 versus 13 days) and hospital stay (15 versus 26 days).

Early diagnosis of IAAL is paramount and it should not be based on clinical suspicion alone. Therefore endoscopic exploration should be performed when possible, allowing early diagnosis, providing information of anastomosis' morphologic characteristics that will help accurate the best management. Eventually treatment can be done at the same time.

Management by a multidisciplinary team, combining endoscopical, surgical and radiological techniques is the best strategy to reduce time until leak healing. It is important to considerate severity and location of the leak as well as the day of appearance. In hemodynamic stable patients, conservative management is effective and can obviate a reintervention, thereby avoiding postoperative complications. Goals are effective drainage, covering dehiscence by an endoscopic stent and renutrition. Endoscopical treatment can heal or may help to make a chronic leak until a definitive surgery can be performed in a patient's optimal clinical and nutritional status.

Hemodynamic unstable patients need a prompt surgical repair. Laparoscopic approach allows evaluation of anastomosis' characteristics, consents a peritoneal lavage and positioning effective drains. Laparotomy remains anecdotal for hemodynamic unstable non-responding patients excluded of mini-invasive treatment, in order to diminish disadvantages and complications of operative treatment.

We suggest applying IAAL definition in forthcoming studies on UGI surgery to homogenise reporting of outcomes thus facilitating comparison of the results from different studies so in the future this concept can be standardize. To conclude, a management algorithm is proposed.

Resumen

Debido al aumento de procedimientos supramesocólicos, especialmente por la cirugía bariátrica, cabe esperar un incremento del número total de sus complicaciones. Entre ellas se encuentra la dehiscencia anastomótica siendo una de las complicaciones más devastadoras, que incrementa la morbi-mortalidad, la tasa de supervivencia a largo plazo y el coste, pudiendo llegar a considerar este evento como un verdadero problema de salud pública. Su incidencia y factores de riesgo están bien descritos en la literatura. Por el contrario, no existe una definición ni tampoco un algoritmo de manejo.

Entre 2003 y 2013, en el CHL, 1.856 pacientes fueron sometidos a una cirugía supramesocólica en CHL: 121 gastrectomías por cáncer (totales: 58 subtotales: 63); 1654 bypass gástrico; y 81 tubuladuras. 15(0.08%) pacientes fueron diagnosticados de dehiscencia anastomótica intraabdominal (10 agudas; 5 crónicas). Se analizó el diagnóstico, el manejo y las complicaciones derivadas de éste.

La dehiscencia anastomótica intraabdominal tras cirugía supramesocólica (IAAL) se definió como la discontinuidad en las anastomosis esófago-yeyunal, gastro-yeyunal o yeyuno-yeyunal, así como en la línea de grapado y los abscesos perianastomóticos descritos en las pruebas de imagen.

El diagnóstico temprano fue posible a un alto índice de sospecha. La identificación de paciente con sepsis severa o shock séptico fue realizada con el sistema de clasificación SIRS. El TAC con contraste oral y/o intravenoso demostró la dehiscencia en 13 pacientes. La endoscopia verificó los hallazgos radiológicos y evaluó el grado de severidad en 9 pacientes. En 5 casos se realizó previo a la cirugía. En este grupo no se evidenciaron diferencias en la tasa de reintervención ni en las complicaciones postoperatorias. Tampoco desarrollaron nuevas dehiscencias posteriormente. Se realizó laparoscopia exploradora diagnóstica urgente en 2 pacientes debido a la inestabilidad hemodinámica.

Se instauró tratamiento precoz combinando técnicas endoscópica, quirúrgicas y/o radiológicas. Las opciones de manejo estuvieron determinadas por la situación hemodinámica del paciente así como por las características de la dehiscencia, para garantizar la nutrición enteral lo antes posible.

Resumen

Cuatro pacientes se manejaron de forma conservadora, curando a 3 de ellos. Once pacientes se trataron quirúrgicamente (8 laparoscópia; 1 laparotomía urgente; 2 cirugía electiva). Ocho pacientes fueron subsidiarios de colocación de stent (tasa de sellado del 62,5%).

Las complicaciones que precisaron manejo en UCI (Clavien-Dindo IV) (33,3%) fueron más frecuentes en el grupo de pacientes con manejo quirúrgico. Un paciente falleció (6,6%). Los pacientes con manejo conservador tuvieron menor estancia media en UCI (10 versus 13 días) y hospitalaria (15 versus 26 días).

El diagnóstico temprano es fundamental y no puede estar basado únicamente en la sospecha clínica. En estos casos se debería realizar una exploración endoscópica. Ello proporciona el diagnóstico precoz, aporta información sobre las características morfológicas de la anastomosis (perfusión tisular, tamaño), que ayudarán a escoger el mejor manejo. Eventualmente, permitiría su tratamiento en el mismo acto.

El manejo por un equipo multidisciplinar combinando técnicas endoscópicas, quirúrgicas y radiológicas es la mejor estrategia para disminuir el tiempo hasta la curación de la dehiscencia. Es importante valorar la severidad, la localización y el día de aparición de la dehiscencia. En pacientes estables hemodinámicamente, el manejo conservador es efectivo y puede evitar la reintervención. Los objetivos son: un drenaje efectivo, cubrir la dehiscencia con un stent y reintroducir la nutrición vía oral lo antes posible. El tratamiento endoscópico puede curar o puede hacer que la dehiscencia sea crónica hasta poder instaurar un tratamiento quirúrgico definitivo cuando las condiciones clínicas y nutricionales del paciente lo permitan.

Los pacientes con inestabilidad hemodinámica necesitan un manejo quirúrgico precoz. El abordaje laparoscópico permite la evaluación de las características de la anastomosis, realizar un lavado de la cavidad peritoneal y la colocación de drenajes efectivos. La laparotomía se limita a casos anecdóticos, pacientes inestables no respondedores excluidos del tratamiento mini-invasivo, para disminuir las complicaciones y desventajas derivadas del tratamiento quirúrgico.

Resumen

Se sugiere la aplicación de la definición IAAL en futuros estudios de cirugía supramesocólica para que los resultados sean homogéneos y así facilitar la comparación de resultados entre los diferentes estudios que más adelante permitan estandarizar este concepto. A modo de conclusión se propone un algoritmo de manejo.

Abreviations

A
AGB: Adjustable gastric banding
ARDS: acute respiratory distress syndrome
ASA: American Society of Anesthesiologists
ASMBS: American Society for Metabollic and Bariatric Surgery

B
BMI: body mass index
BPD/DS: Biliopancreatic diversion/duodenal switch
bpm: beats per minute
bpm: breaths per minute

C
CHL: Centre Hospitalier de Luxembourg
cm: centimeters
CR: case report
CRP: C reactive protein
CT: Computed Tomography

D
DIC: disseminated intravascular coagulation
dL: deciliters
DM: diabetes mellitus
e.g.: example given

E
E-PASS: Estimation of Physiologic Ability and Surgical Stress
EGJ: esophagogastric junction
EJA: esophago-jejunal anastomosis
EJAL: esophago-jejunal anastomosis leak

F
F: female
FDA: Food and Drug Administration
Fr: French
FS: fibrin sealants
FSEMS: fully covered self-expanding metal stent

G
g: gram
GBP: gastric bypass
GEJ: gastro-esophageal junction
GI: gastrointestinal
GJ: gastro-jejunal
GJA: gastro-jejunal anastomosis
GJAL: gastro-jejunal anastomosis leak
G95%: 95% oncologic gastrectomy or near total gastrectomy

I
IAA: intraabdominal abscess
IAAL: intraabdominal anastomotic leak
ICU: intensive care unit
IQR: interquartile range

J
JJ: jejun-jejunal
JJA: jejuno-jejunal anastomosis
JJAL: jejuno-jejunal anastomosis leak

K
kg: kilogram

L
LGBP: laparoscopic gastric bypass
LSG: laparoscopic Sleeve Gastrectomy
LSTG: laparoscopic subtotal gastrectomy
LTG: laparoscopic total gastrectomy

M
m: meter
M: male
mg: miligrams
mm: milimeters
mm^3: cubic milimeter
MOF: multiorganic failure

O
OAD: oral antidiabetic drugs
OSA: Obstructive Sleep Apnea

P
P: prospective
PCT: procalcitonin
POD: postoperative day
PSEMS: partially covered self-expanding stent

R
Retros: retrospective
RF: renal failure
RYGBP: Roux-en-Y gastric bypass

S
SD: standard desviation
SEMSs: self-expandable metal stents
SEPS: self expandable plastic stent
SESs: self-expandable stents
SG: sleeve gastrectomy
SIRS: systemic inflammatory response syndrome
SReview: systematic review

T
TG: total gastrectomy

U
UGI: upper gastrointestinal
US: ultrasound
UTI: urinary tract infection

V
VAC: vacuum assisted closure
VAS: visual analogue scale

W
WBC: white blood cell

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introduction

Biliary, pancreatic and colorrectal leak is a concept well defined in the literature. Authors have reached a consensus, standardized diagnostic algorithms and severity degrees. The implementation of uniform definitions of anastomotic leak enables surgeons to compare and to improve treatments' options. Nevertheless comparable consensus definitions for leaks in esophago-jejunal anastomosis (EJAL), gastro-jejunal anastomosis (GJAL) or following small bowel anastomosis have not been established.[1] In spite of the fact that there are different surgical techniques for the upper gastrointestinal (UGI) tract where the gastrointestinal anastomosis vary considerably there are common and general concepts for diagnosis and management.

1.1. CURRENT STATUS

Surgery is the only curative treatment for gastric cancer and the most effective and cost-effective treatment for morbid obesity [2] allowing a ponderal reduction and its long term maintenance, decreasing up to one third of the global mortality (due to cancer and cardiovascular pathologies), respiratory diseases and quality of life as well as resolution of the clinical manifestations of type 2 diabetes or its improvement.[3-7]

In 2009, approximately of 350 surgical intestinal actions, 2 over 10 did not have anastomosis neither sutures in France.[8] The recent improvement of laparoscopic approach, which requires automatic devices for sutures and anastomosis, has determined modifications in many surgical practices, specially in gastric surgery.[8] Industries' recent development of the automatic suturing devices and its increased use in anastomosis in the GI tract, has achieved a marked reduction in EJAL.[9,10] But the multiplying number of procedures, especially due to bariatric surgery, entails an expected increase in the absolute number of surgical complications.[2] French National Surgery Annual Report of 2009 reveals that 5,666 gastrectomies were performed in 2006: 2,393 (42%) partial gastrectomies, 1,691 (30%) total gastrectomies and 1,225 (22%) atypical resections; that year 12% of the gastrectomies were done by laparoscopy.[8]

Bariatric procedures are among the most commonly performed gastrointestinal operations today.[11] A bariatric surgery worldwide survey in 2011 calculated the global total number of procedures in 2011 was 340,768. The most commonly performed procedures were:

- Roux-en-Y gastric bypass (RYGBP) 46.6%
- Sleeve gastrectomy (SG) 27.8%
- Adjustable gastric banding (AGB) 17.8%
- Biliopancreatic diversion/duodenal switch (BPD/DS) 2.2%

The global trends from 2003 to 2008 to 2011 *(figure 1)* showed a decrease in RYGB (65.1 to 49.0 to 46.6%) and a marked increase in SG (0.0 to 5.3 to 27.89%); BPD/DS declined (6.1 to 4.9 to 2.1 9%); USA/Canada performed the largest number of operations (101,645), followed by Brazil (65,000), France (27,648), Mexico (19,000), Australia and New Zealand (12,000), and the UK (10,000). No other nation performed 10,000 or more operations.[11]

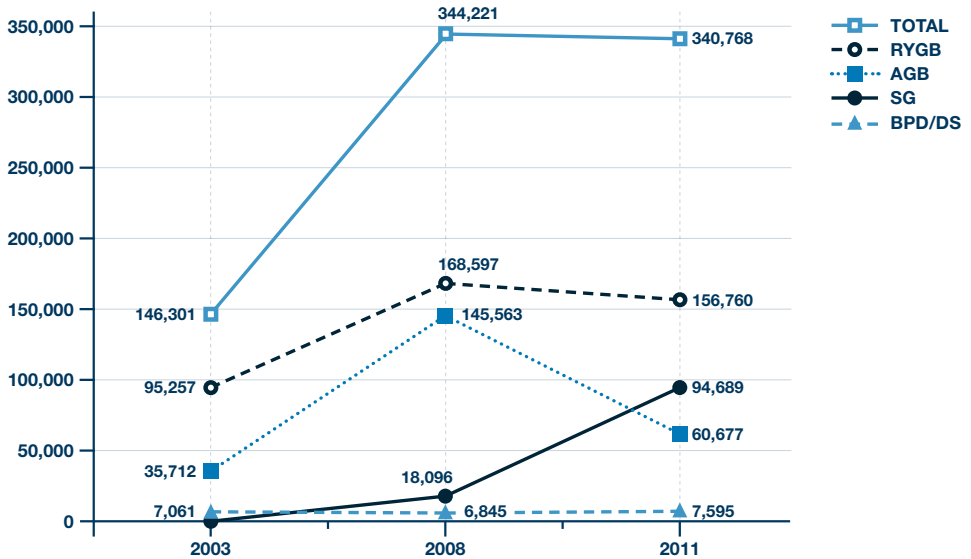

Figure 1: Trends in numbers of bariatric procedures worldwide: 2003 to 2011. [11]

INCIDENCE DATA

EJAL rate vary from 0 to 26% with an average of 5-8% in major recent series.[12] In bariatric surgery the global incidence average is around 3%. Leak rates after laparoscopic gastric bypass (LGBP) vary from 0 to 5.6% in major series and despite some authors conclude that there are no differences between laparoscopy and standard approach,[13] others conclude that leak rate was significantly lower in laparoscopic compared with open GBP (0.3% vs. 2.0%, $P < .01$).[14]

There are four potential sites of anastomotic leak after Roux-en-Y LGBP *(figure 2)*: at the GJA, the gastric pouch staple line, the gastric remnant staple line and the JJA. The frequency with which leaks occur is not specified in most studies. The study from Ballesta and collegues [15] reported their experience regarding bariatric leaks with their specific location: 68% at the GJA, 10% at the gastric pouch staple line, 3% at the remnant gastric staple line, 5% at the JJA and the remaining 14% at combinations of these. In general, it is accepted that the GJA is the most site prone to leak, because is the most noted site in many large series.[2]

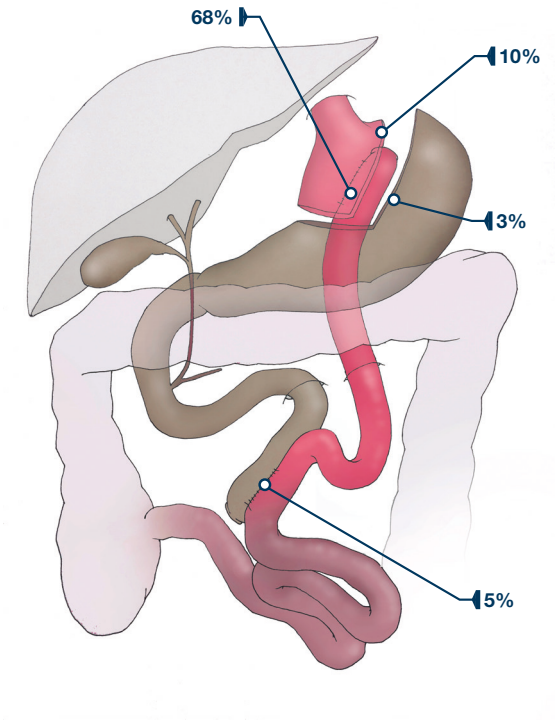

Figure 2: Location of staple line leaks after Roux-en-Y gastric bypass of Ballesta and cols.[15] The remaining 14% were combinations of these.

Leak rate after laparoscopic sleeve gastrectomy (LSG) fluctuates between 0 and 7%.[16,17] There does appear to be a higher leak rate in patients with a BMI>50 kg/m^2.[18] It is frequently located at the proximal portion of the staple line, in the esophagogastric junction (EGJ) because this part is thinner than the rest of the stomach wall.[16] Elariny et al [19] demonstrated that the stomach has different thickness throughout with the fundus being the thinnest at approximately 1.7mm.

MORBIDITY AND MORTALITY DATA

Even though surgical complications and mortality rate for gastric cancer have significantly decreased over the past years, they are still considered high.[20] Anastomotic leak rate is higher for total gastrectomies than for partial ones. The adjusted 30-day mortality rate is Europe is higher in the Netherlands (6.9%), Sweden (3.5%) and Denmark (4.3%).[21]

Anastomotic leakage after gastric cancer surgery is the most devastating complication and an independent prognostic factor for long-term survival in patients with gastric cancer.[22] It also entails a reduction in patients' quality of life, a longer hospital stay, higher hospital costs and a higher mortality rate,[12] which ranges from 25 to 75%.[23]

In relation with bariatric surgery contradictory data have been reported on mortality rates and it depends on the population under the study, the type of intervention and the characteristics of the institutions involved.[24] The retrospective review done by Kohnet et al [25] over 100,000 procedures in the USA between 1998 and 2006, revealed a mortality rate lower than 0.2%. It was statistically related with the number of cases per year per surgeon and the type of intervention (higher mortality in the case of malabsorptive techniques and lower in laparoscopic gastric banding). Post-surgical leaks produce a 2-fold increase in mortality and 6-times increase in hospital stay compared with patients without leaks.[2] It is the second cause of death after pulmonary embolism, and both of them are responsible of more than 50% of deaths in patients with bariatric surgery.[13] Patients who develop leakage during the hospital stay have higher incidence of surgical site infection, sepsis, embolic events, internal hernias, bowel obstruction and renal and respiratory failure than those who do not develop this complication.[26]

1.2. RISK FACTORS

Causes are not well defined neither for benign and malignant disease.[2] *Table 1* summarizes anastomotic leak risk factors after gastric surgery for cancer published in larger series. There is still controversy about the nutritional status, presence of diabetes, surgeon experience and type of reconstruction.

Table 1: Risk factors for IAAL after gastric surgery for cancer (controversial factors are shaded).
Migita [10] - Deguchi [27] - Sierzega [12] - Nagasako [22]

Patient Related	Surgery Related
Hb A_{1c} > 7 [10]	Intraoperative technical mistake [10,22]
Renal insufficiency [10]	Prolonged surgical time [10,27]
Pulmonary insufficiency [27]	Splenectomy [12]
Cardio-pulmonary preoperatory status [12]	
Diabetes Mellitus [10]	Surgeon's experience [10]
Malnutrition [12]	Type of reconstruction [27]
Obesity [12]	

Leak risk factors after bariatric surgery have been more studied. The increased number of procedures performed allows studying large series and having conclusions statistically significant that are exposed on *table 2*. We can summarize that prevention of leak depends on the strict patient selection and accurate surgical tecnique.[28] In the other hand, there are prospective studies that conclude that the incidence of staple-line leaks appears to be independent of the number of LGBP performed.[29]

Table 2: Risk factors for IAAL after bariatric surgery (controversial factors are shaded)
Morales [2] - Kahn [30] - Griffith [31] - González [32] - Aurora [16] - Harakeh [13]

Patient Related	Surgery Related
> 45 years [2,30]	Revisional surgery [32]
Men [2,30,32]	Open surgery [30]
BMI > 50 kg/m² [30,32]	Surgeon's experience [31]
Obstructive Sleep Apnea (OSA) [2,30]	Non standardized technique [32]
Arterial hypertension [32]	Ischemic tissues [2]
Comorbilities [32]	Anatomic variabilities [2]
Previous abdominal surgery [32]	Non tension-free anastomosis [2]
Recent cardiac disease [30]	Bougie size >40-Fr [16]
DM in treatment with OADs [30]	Staple height [2, 16]
Ascites [30]	Fibrin sealant [13]
Corticotherapy [30]	

1.3. PHYSIOPATHOLOGY AND BIOMECHANICS OF STAPLING

There are many causes of staple-line leaks but Baker [33] summarizes it in two categories: mechanical/tissue causes and ischemic causes. In both cases, intraluminal pressure exceeds the strength of the tissue and the staple-line, resulting in a leak. Classic ischemic leaks are described to occur 5-7 days postoperatively when the wound healing is between the inflammatory and fibrosis phases. In their

clinical experience and in their literature review, they observe that the vast majority of leaks occurred in the first two days following surgery. During the reoperation they did not see evidence of ischemia but instead found evidence of staple-line failure in well-perfused tissue. Therefore they believe that most leaks are due to mechanical/tissue issue and that true ischemic leaks are rare.[33]

The diverse staple cartridges are designed for different tissue thickness to allow tissue apposition, hemostasis while avoiding significant ischemia and tissue destruction.[33] Human tissues are considered biphasic because of their liquid and solid components. The intra and extra-cellular fluids components influence the tissue, so that elongation (tissue creep) occurs when crushing force is applied. When subjected to an applied displacement, stress relaxation occurs. At some point, increasing compression will produce excess tissue shear or tensile stress that results in tearing of tissues. The phenomena of tissue creep, stress relaxation, and shear or tensile stress are dependant upon one common factor: time.[33] Optimal stapling then would consist of allowing adequate time for tissue compression and creep while not producing excessive tensile stress.[34]

Different studies were made to determine the optimal pressures; they were found to be 8 g/m^2 for gastric tissue and 6 g/m^2 for the esophagus or intestines. The results demonstrated that optimal pressure when applied, caused good apposition and negligent structural modifications with no long-term tissue disruption or aggravation.[35]

1.4. CLINICAL FEATURES

Depending on the anastomotic leak location, time to diagnosis and time to establishment of treatment it may have a different clinical presentation with diverse systemic repercussion (e.g. peritonitis and/or septic symptoms and signs, biliary or intestinal drainage). There is a discrepancy between severity and lacking symptoms in bariatric patients, hence surgeon has to keep a high suspicion to identify and diagnose this complication.[28]

In contrast to non-obese population, bariatric patients with leak often present without fever, leukocytosis, or abdominal pain. In many patients the only sign is sustained tachycardia.[2] Gonzalez and

collegues [32] reported that tachycardia (>100 bpm) was the only consistently present indicator in 72% of patients with a confirmed anastomotic leak; fever and leukocytosis was present in 72% and 42% respectively. Carruci et al [36] also noted that the most common symptoms after tachycardia (92%) were nausea and vomiting (81%) in the study group.

For Guirao et al [37] the prompt diagnosis of severity in patients with intraabdominal infection and the early treatment with antibiotics is related to a better prognosis in severe intraabdominal infection. To that end they propose a simple classification of the systemic inflammatory response syndrome (SIRS) that can be obtained easily on the bedside of the patient *(Table 3)*. They have demonstrated its utility in identification of severe sepsis and septic shock remarking a good correlation between mortality rate in patients with severe sepsis.

Table 3: SIRS criteria and evaluation of severity in intraabdominal infection. [37]

SIRS (2 or more of these criteria)	
Temperature > 38º or <36º C **Heart rate > 90 bpm** **Respiratory rate >20 breaths per minute** **White blood cell count >12,000 l/mm³ or < 4,000 l/mm³ or >10% band neutrophils**	
Mild-moderate intraabdominal infection	**Severe intraabdominal infection**
SIRS with venous lactate ≤ 2 mmol/l	**Presence of 4 criteria de SIRS** or **SIRS with 1 organ failure *(severe sepsis)*** or **Hypotension requiring vasoactive drugs *(septic shock)*** or **Venous lactate >2 mmol/l**

1.5. DIAGNOSIS

Running time between anastomotic leak and treatment establishment, endoscopic or surgical, is one of the most critical prognostic factors.[38] Early detection and immediate adequate treatment are the most important factors for a favorable outcome. Delayed diagnosis is associated with a high risk of abdominal collection, sepsis and treatment failure.[39]

There are several options varying from the less invasive exams like CT scan with oral contrast, esophagogram with oral contrast and blue methylene; to more aggressive, like exploratory laparoscopy or laparotomy. More recently the role of endoscopy is getting defined for the diagnosis of

anastomotic leaks after UGI surgery. Summarising, patient's hemodynamic status is going to determine the diagnostic method of IAAL.

1.6. PRINCIPLES OF TREATMENT

Management of IAAL after UGI surgery is not well defined in literature and may change from one group to another and depends also on the first surgery. Csendes and colleagues in the early '90s settle the basis of non-operative treatment in EJAL that later Lang and colleagues [40] in 2000 ratify, concluding that conservative treatment with a naso-intestinal tube and percutaneous drainage of intraabdominal abscesses is realistic for anastomotic leak.

Nowadays there are described different treatment options: laparoscopic/laparotomy urgent surgical exploration (washing and drain, discontinuity and resection, diversion, re-anastomosis); conservative treatment with broad-spectrum antibiotics, percutaneous drain, enteral/parenteral nutrition and naso-intestinal tube. As a principle anastomotic leak treatment must be multidisciplinary, must be done as soon as possible and will depend on patient's clinical and/or hemodynamic conditions. Hemodynamically unstable patients with anastomotic leak are susceptible to a more aggressive treatment while patients with a scarce clinical repercussion will profit of a conservative treatment or an observing attitude.

Both surgical and non-operative treatment are associated with high mortality rates and long intensive care unit and hospital stays. In the search for an optimized management, the endoscopic placement of stents has been introduced in the management of anastomotic leakages in the past decade.[41-44] The use of self-expandable metal stents (SEMS) is well established in the palliative treatment of patients with an upper GI neoplasm or tracheo-esophageal fistula.[45]

Stents are capable to effectively seal leaks while they protect the bowel mucosal wall at the same time that healing takes place when an effective drain is deployed.[46] The retrieval after temporary therapeutic use has not been reasonably possible until the development of covered stents. It can be removed 4 to 6 weeks after, once sealing of the leak is confirmed with a radiological test (transit or CT scan with oral contrast).[39,45] This has opened a pathway for new therapeutic strategies [47]

reported in literature as cases and short series with promising results; the disadvantages are that they are small, heterogeneous, non randomized cohorts.[45] The main drawbacks are stent migration and tissue in or over-growth, both of which need a repeated intervention.[38] There are multiple types available *(table 4)* from various enterprises that differ on the material they are made of, design, luminal diameter, radial force exerted, flexibility and degree of shortening after use.[48]

Other encouraging endoscopical treatments recently published have been: endoscopic clips, vicryl plugs and fibrin sealants (FS) injections and argon plasma endoscopical treatments.[15,49-59]

Table 4: Stents and their characteristics

Type			Characteristics	Commercial names
SEMS	**Metallic**		Stainless steel or nitinol (alloy of nickel and titanium with a thermic memory) [60] Inert, resistant to corrosion [60] Non allergenic (can be placed in patients allergic to nickel) [60] Induces an inflammatory fibrotic response that reduces the risk of migration [60]	
	Uncovered (SEMS)		Main drawback: tissue growthàcan make removal difficult Generally used in palliative treatment	Wallflex-Ultraflex-(Boston) Evolution (Cook)
	Covered		Silicon or polyurethane Main inconvenient: migration	
		Partially	Usually with wide endings not covered that help endoluminal fixation [60] First therapeutic option for anastomotic leaks [60]	Wallflex (Boston) Osiris (ABS-Bolton) Hanaro stent (Life Europe)
		Fully	Recently approved by the FDA [38] Potentially associated with increased risk of migration [38] Published data are awaited [38]	HV stent (ABS- Bolton)
SEPS	**Plastic**		Polyurethane Conceived to prevent mucosal proliferation, tracheo-oesophageal fistula and strictures [61] Require clips or suturing to guarantee its position despite a proximal widening [62] Highest migration rate [61] Similar healing time (80-90%) [61] Low mortality-related leak rates [61]	Polyflex (Boston)

1.7. OBJECTIVES

The aims of this study are to:

- Propose a definition of intraabdominal anastomotic leak after UGI surgery.
- Establish incidence in our center.
- Describe our surgical techniques for anastomosis in the UGI tract.
- Describe the spectrum of clinical presentations, use and efficacy of diagnostic exams.
- Describe our management and results, and compare them to international reference series.
- Propose a flowchart algorithm for its treatment.

material and methods

2.1. PATIENTS

A retrospective review was made in the prospective database of the patients submitted to an UGI surgery at Centre Hospitalier of Luxembourg (CHL) between January 2003 and April 2013. Patients with an IAAL were identified and included in this study. Information obtained from hospital records to describe patients, clinical presentation, diagnosis and management was collected:

- **Patient data**: age, sex, BMI, comorbilities, leak location, previous surgery done outside CHL, preoperative treatment (neoadjuvant treatment), type of anastomosis, margin borders affection if malignancy.
- **Diagnosis**: symptoms and signs (fever, pain, heart rate, respiratory rate, peritonism, MOF, drain); laboratory variables (WBC count, CRP, procalcitonine); diagnosis exam (thorax Rx, blue of methylene, CT scan with oral and intravenous contrast, diagnostic laparoscopy or laparotomy); diagnostic sequence.
- **Treatment**: reoperation, number of reinterventions, surgery done the second time, placement of percutaneous drain, stent, clip, fibrin sealant, time to healing.
- **Complications**: they were classified using the Clavien-Dindo classification [63,64] *(see appendix A)*.
- **Hospital admission**: admission in intensive care unit, hospital admission.

2.2. DEFINITION OF INTRAABDOMINAL ANASTOMOTIC LEAK AFTER UPPER GASTROINTESTINAL SURGERY

Anastomotic leak was defined as a disruption on the staple line and/or a disruption of the EJA, GJA and JJA. It was also considered as an anastomotic leak the para-anastomotic abscesses seen on radiological images, although communication to anastomosis could not be seen with oral contrast. They were classified regarding to:

- **Time of appearance after sugery**: intraoperative, acute (1-11 days after surgery) or chronic (12 or more days after surgery).[50]
- **Hemodynamic stability of the patient**: stable, unstable.
- **Anatomic location**: staple line, EJA, GJA and JJA.
- **Morphological characteristics founded in endoscopy**: total wall necrosis, circumference defect <70% or >70%.

2.3. SURGICAL TECHNIQUES

Nowadays our surgical techniques are standardized and some of them have been described in different published papers and videos. We detail below the technical aspects of the different procedures, starting with the **total gastrectomy full-laparoscopic approach (LTG)** for cancer.[65–67]

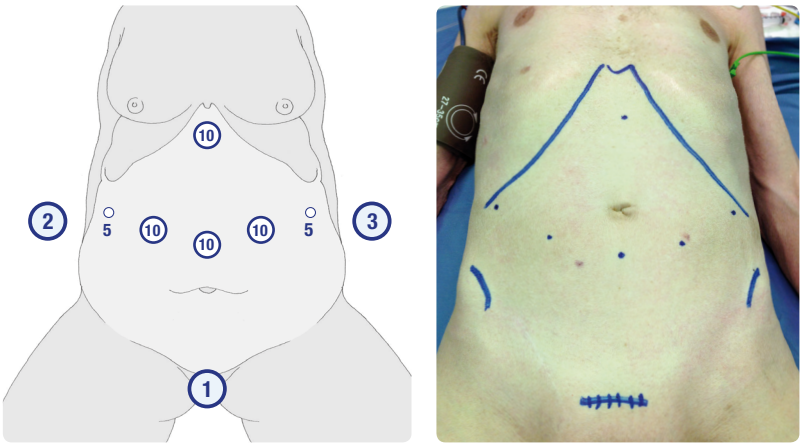

Figure 3: Trocar position for laparoscopic total gasterctomy.

It is accomplished with ports as *figure 3* shows. Duodenal section is made 2 cm distal to pylorus with a 60mm Echelon ® Flex 1.5 mm staple (blue cartridge) without over sewing the staple line, unless intraoperative active bleeding is seen. After proceeding with the anatomical dissection and D2 lymphadenectomy, the esophageal section is made 2 cm below the cardias with a 60mm Echelon ® Flex 1.5 mm staple (blue cartridge) *(figure 4)*.

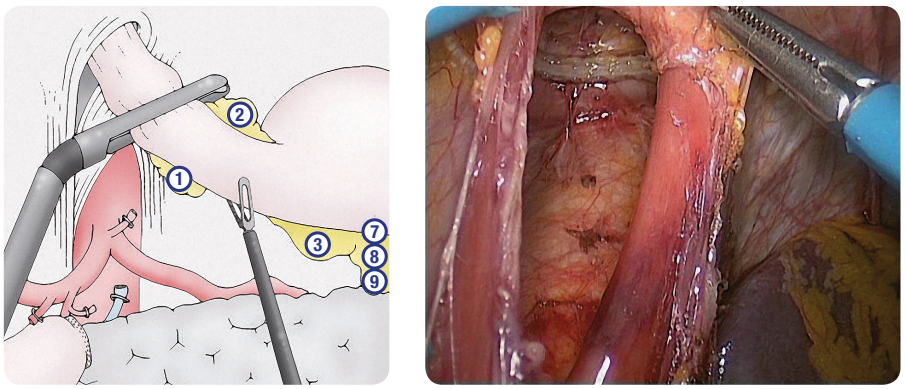

Figure 4: Schematic representation and laparoscopic view of esophageal section in laparoscopic total gastrectomy. **1:** Right paracardial lymph nodes **2:** Left paracardial lymph nodes **3:** Lesser curvature lymph nodes **7:** Left gastric artery lymph nodes **8:** Common hepatic artery lymph nodes **9:** Celiac artery lymph nodes

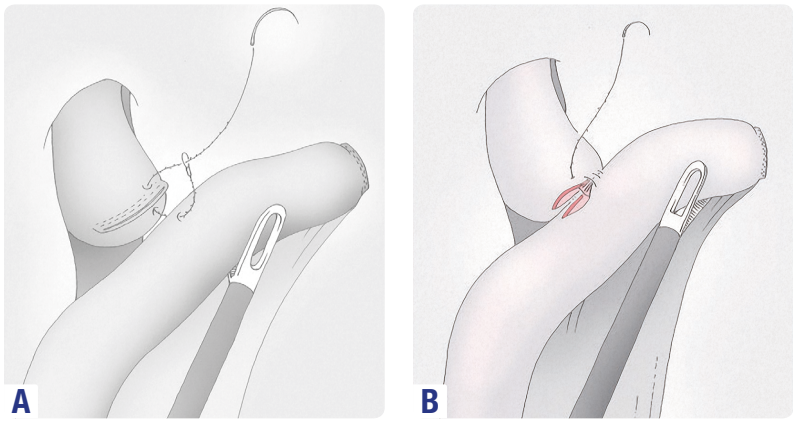

Figure 5: Design of gastroyeyunal anastomosis performed with barbed suture. **A**: posterior plane **B**: anterior plan

Manual intracorporeal EJA is made with barbed suture. Starting the posterior layer in the left of the esophageal staple line, it is achieved by a locking suture of a 15cm V-Loc® (Covidien, United Kingdom). Taking the esophageal staple line early in the suture a full-thickness stitch both in jejunum and esophagus is done *(figure 5)*. When the suture is completed, the wire is cut without a knot, with a tail of 1.5 cm. An optional reinforcement of this layer can de made with simple reabsorbable stitches, to optimize and bind the protuberant intestinal mucosa. Anterior layer starts from the left at the first stitch of the posterior suture and fixes the jejunum to the esophagus with large extramucosal stitches. Suture ends beyond the end of the posterior suture and the wire is then cut without a knot with a tail of 1.5 cm. Check of sealing is made optionally.

Fifty centimeters below EJA, Roux-en-Y mechanical side-to-side JJA is made with a 60mm Echelon ® Flex 1.5 mm staple (blue cartridge). Defect for introduction of the stapler is closed indistinctly manually, with a barbed suture or mechanical. Afterwards the alimentary limb is fixed to the left diaphragmatic pillar.

Non-aspirative drain is left systematically under posterior face of EJA. Specimen is removed by a Pfannenstiel incision. Both naso-gastric tube and epidural analgesic are placed if necessary. ICU surveillance is made during the first 24-48 hours. A negative transit made systematically on the 5th postoperative day (POD) and if there is no evidence of leak or obstruction, oral intake is started.

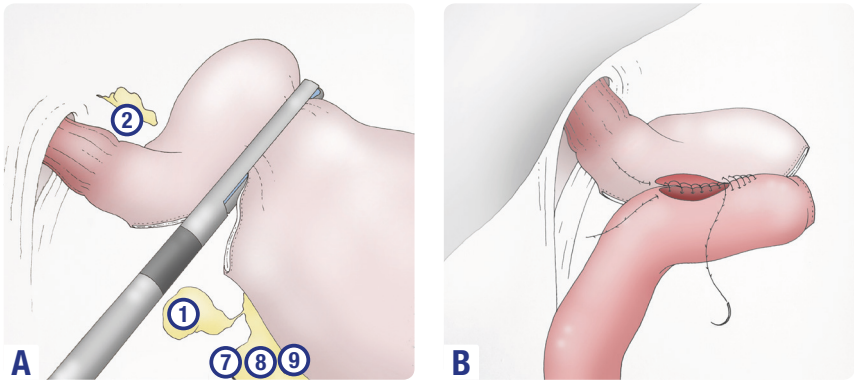

Figure 6: Schema of laparoscopic subtotal gastectomy.
A: gastric section **B**: completion of anterior plane of gastro-yeyunal anastomosis with barbed suture.
1: Right paracardial lymph nodes **2:** Left paracardial lymph nodes **7:** Left gastric artery lymph nodes **8:** Common hepatic artery lymph nodes **9:** Celiac artery lymph nodes

For **subtotal gastrectomy full laparoscopic approach** (LSTG) *(figure 6)* gastric section is made with automatic devices (60mm Echelon ® Flex 1.5 mm staple -blue cartridge-) in the union of the proximal fifth with the distal four fifths. Staple line is over-sewed with a barbed suture (V-loc®). Manual end-to-side GJA is made with a barbed suture and also can be reinforced in the posterior face with vycril stitches. Roux-en-Y JJA, drains, naso-gastric tube, epidural analgesic and ICU surveillance is made as explained before. Oral intake is started the 3rd POD if there are no postoperative problems.

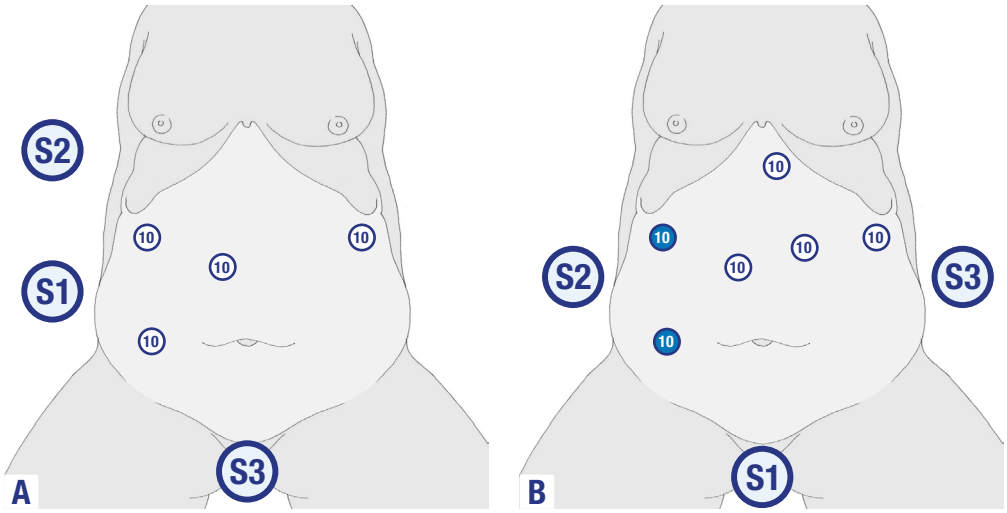

Figure 7: Trocar position for laparoscopic gastric bypass. **A**: inframesocolic step **B**: supramesocolic step.

Preoperatory endoscopy was performed in all patients with benign disease or morbid obesity undergoing surgery. Our group performs **Roux-en-Y laparoscopic gastric bypass** [68,69] retro-gastric and transmesocolic *(figures 7, 8)*. A 2.8 cm mechanical (Echelon ® Flex 60 mm 1.5 mm cartridge) side-to-side isoperistaltic GJA is made closing the orifice with a barbed suture (V-loc®). Roux-en-Y JJA is made as described before. Naso-gastric tube and drain guarding GJA are selectively placed.

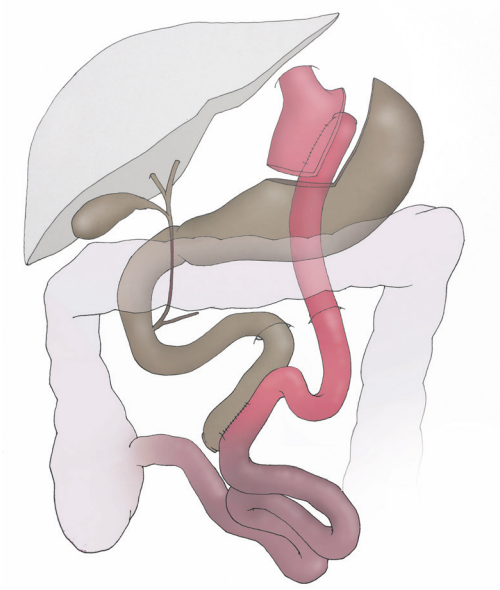

Figure 8: Gastric bypass carried out by our group: retrogastric and transmesocolic.

For **laparoscopic Sleeve Gastrectomy (LSG)** [70] *(figure 9)* the gastroepiploic ligament section is made from 7 cm proximal to the pylorus until Hiss angle with an ultrasonic device (Harmonic Ace®). A 32 Fr Faucher tube calibrates and mechanical section (Echelon ® Flex 60 mm) is made; the first two cartridges are 1.8mm and the others are 1.5mm. Staple line is over sewed with a barbed suture (V-loc®) if necessary (e.g. bleeding); naso-gastric tube and drains similarly. Morbid obese patients with OSA are monitorized in ICU during at least 24 hours.

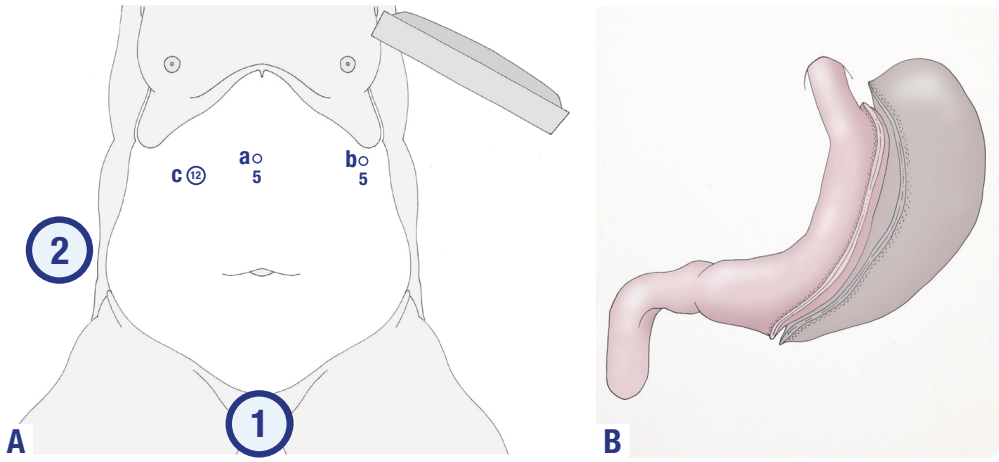

Figure 9: Trocar position and representation of laparoscopic sleeve gastrectomy.

Postoperative care is standardized in all patients and includes subcutaneous low molecular weight heparin and proton pump inhibitors for the first postoperative month. No routinely radiological series after bariatric surgery are performed; as opposed to the systematically upper gastrointestinal series (UGS) with water-soluble contrast swallow who are done on the 5th POD systematically after LTG. If the contrast passed through the bowel and there was no evidence of leak or obstruction, the patients' diet was advanced. The patients after bariatric surgery were discharged on postoperative day 3 or 4 while after surgery for cancer was on 7th to 10th POD. Drainage was removed (when present) on postoperative days 4-8.

2.4. DIAGNOSIS

Upper gastrointestinal series (UGS) with water-soluble contrast swallow are done on the 5th POD systematically after LTG. In contrast to previous, after bariatric surgery, necessity of diagnostic exams is determined by clinical symptoms and/or exploration.[71] In **hemodynamic stable** patients with tachycardia, nausea, vomiting or abnormal postoperative evolution with or without abdominal pain a CT scan with oral and intravenous contrast is made. Nowadays the first diagnosis tool used in these cases, when possible, is an endoscopic exploration. The location, size (expressed in percentage of circumference) and perfusion of the anastomosis are verified. If necessary, an endoscopic treatment would be performed.

Exploratory laparoscopy or laparotomy is the diagnostic method in **hemodynamic unstable** patients, that allows at the same time treatment. Optimizing treatment in ICU is done whenever possible.

2.5. CONSERVATIVE MANAGEMENT

Conservative treatment consists of broad-spectrum antibiotics, nutritional support and effective drain of collections (US or CT-guided). Oral feeding is started afterwards. CT scan with oral contrast evaluates leak closure and withdrawal of the drain 7-10 days after treatment instauration.

2.6. SURGICAL MANAGEMENT

When surgery was needed reoperation was done by laparoscopy, if possible, or laparotomy. Anastomosis is verified looking for complete dehiscence and transmural necrosis. When urgent reintervention is necessary, in absence of previous signs, peritoneal washout, aspiration and effective drain placement around anastomosis is done. Rarely reinforcement stitches in the anastomosis can be made, due to the inflammation process. If there is a complete dehiscence reconstruction or diversion of the GI tract are considered.

Commonly late postoperative leaks allow elective surgery once the inflammation process is under control, granting a reconstruction of the anastomosis in safety conditions.

2.7. ENDOSCOPICAL TREATMENT

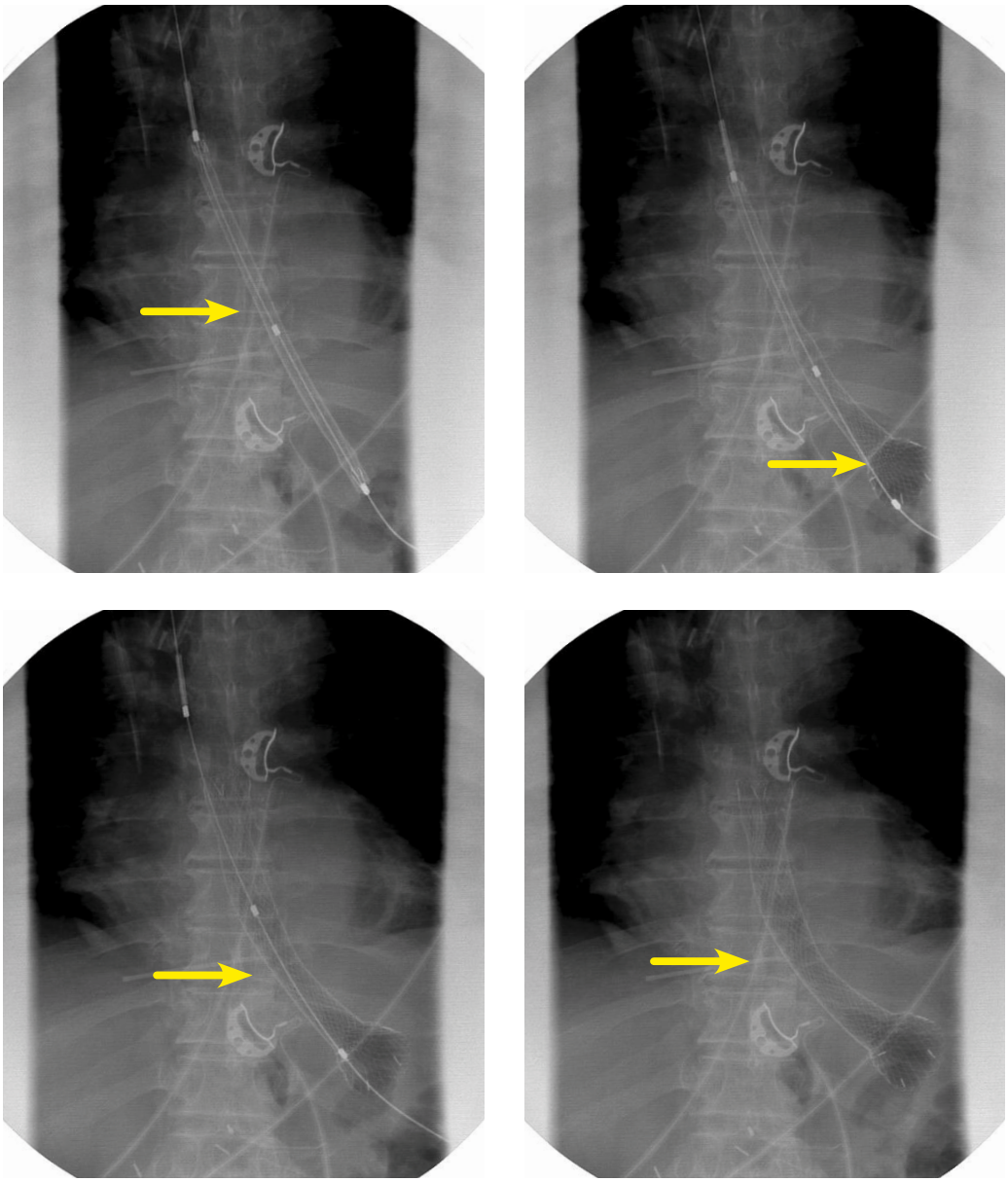

Figure 10 : Deployement of stent under fluoroscopy in an EJ anastomotic leak.

Patients who submitted endoscopic exploration and had no transmural necrosis and a less than 70% of the circumference anastomosis defect are candidates for stent. In our center SEMS covered (Ultraflex®, Boston Scientific, USA) were deployed under endoscopy or fluoroscopy *(figure 10)*.

An UGI transit with oral contrast is made after 24 hours and if leak is sealed oral intake is started, progressing to a diet as patients without leak if there is a good tolerance *(figure 11)*. At this point patients are discharged. During this period if there is abdominal pain or dysphagia a CT scan or transit is made to verify the stent position.

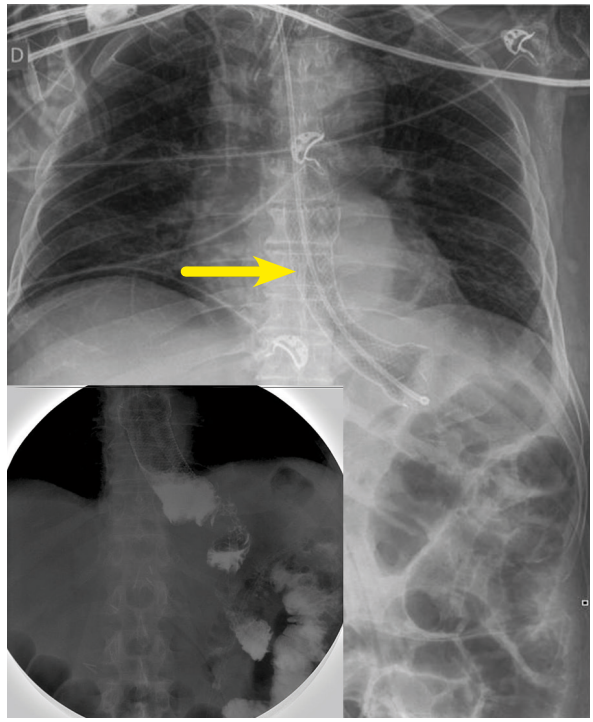

Figure 11: SEMS covered (Ultraflex®, Boston Scientific, USA) is deployed under fluoroscopy in an EJAL. Transit with oral contrast made after 24 hours shows leak sealed. Oral taken is started afterwards.

Stents are left in place (if well tolerated) 6 weeks. A transit with oral contrast is made before withdrawal to ensure leak closure.

2.8. LITERATURE SEARCH

Literature review was performed in electronic data bases Pub Med, Up to Date, Clinical Key, Cochrane and also in Google Academic using a combination of keywords: “morbid obesity”; “gastric cancer”; “laparoscopy”; “laparoscopic Roux-en-Y gastric bypass”; “laparoscopic sleeve gastrectomy”; “gastrectomy”; “complications”; “anastomotic leak”; “risk factors”; “outcomes”; “morbidity”; “mortality”; “reoperation”; “sepsis”; “endoscopy”; “stent”; “repositionable”; “self-expandable metallic stent”; “Clavien-Dindo

classification"; "enteral nutrition"; "nasointestinal tube"; "length of stay". Boolean operators (NOT, AND, OR) were used, when appropriate, to widen or narrow the search. A selection of the potential relevant articles was done after reading the abstracts; this assortment was completely reviewed. No meta-analysis was carried out to combine the results of the different studies, due to global heterogeneity.

2.9. STATISTICAL ANALYSIS

We presented continuous data as mean and standard deviation or median and interquartile range (IQR) or extreme values. When comparing two groups, we used the Student *t* test for normally distributed data; otherwise, the nonparametric Mann-Whitney *U* test was used. For proportions, we used the Pearson $\chi 2$ test or the Fisher exact test for scarce data. We evaluated assumptions for all statistical models and found none were violated. We considered $P < .05$ as statistically significant; all statistical tests were 2-sided. We used IBM SPSS Statistics software package version 14.0 (IBM España S.A., Madrid) for statistical analysis.

results

Between January 2003 and April 2013 1,856 patients underwent a supramesocolic laparoscopy surgery in Centre Hospitalier of Luxembourg: 121 gastrectomies for cancer (LTG: 58 and LSTG: 63); 1654 LGBP; and 81 LSG. Postoperative leak was diagnosed in 15(0.8%) patients *(figure 12)*. *Table 5* summarizes patients diagnosed and treated in our center.

Table 5: Patients diagnosed of IAAL after an UGI surgery at Centre Hospitalier of Luxembourg. (**M**: male - **F**: female - **A**: acute - **C**: chronic)

Patient	Gender	Age	BMI (kg/m^2)	Surgical Procedure	IAAL location	Time of appearance
1	M	74	26	LTG	EJA	A
2	M	73	29	LTG	EJA	A
3	M	72	22	LTG	Duodenal stump	A
4	M	48	24	Roux-en-Y Antrectomy	GJA	C
5	F	29	41	LSG	Hiss angle	A
6	F	27	40	LSG	Superior third staple line	C
7	M	23	40	LSG	Hiss angle	C
8	F	31	43	LGBP	GJA	A
9	F	61	40	LGBP	GJA	A
10	F	48	42	LGBP	GJA	A
11	F	37	42	LGBP	GJA	A
12	F	25	39	LGBP	GJA	A
13	M	30	42	LGBP	Hiss angle	C
14	M	41	50	LGBP	GJA - Gastric remnant	A
15	F	51	53	LGBP	JJA	C

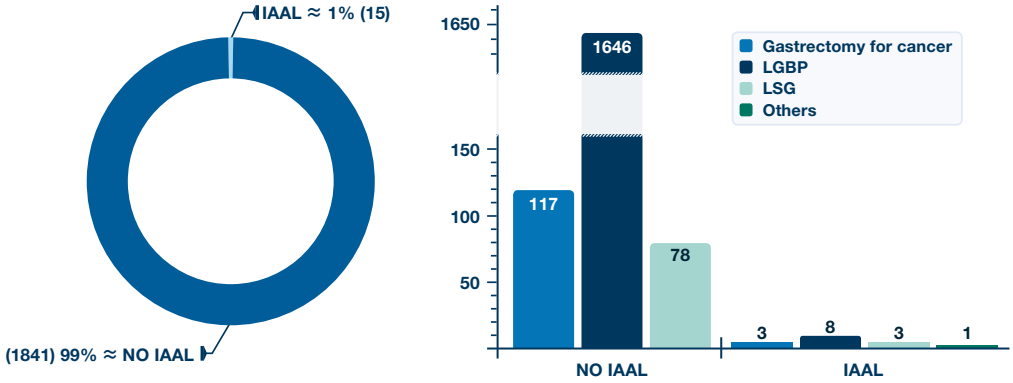

Figure 12: Representation of IAAL rate (0.8%) after upper GI surgery in CHL.

3.1. EPIDEMIOLOGICAL CHARACTERISTICS

Table 6: Epidemiological characteristics

	NO LEAK *(99.2%)* N=1841	LEAK *(0.8%)* N=15
Malign process	117	3
Benign process	1724	12
Gender		
Female	1112 (60.4%)	8 (53.3%)
Male	729 (39.6%)	7 (46.7%)
Age (years) median (range)		
Malign process	67 (36-82)	73 (72-74)
Benign process	39 (13-68)	37.5 (23-61)
BMI (kg/m²) median (range)		
Malign process	26 (21-32)	25.6 (22-29)
Benign process	49 (39-70)	41.3 (24-53)
Death (leak related)	1	1

Table 6 shows the epidemiological characteristics of all patients. In the group of patients with leaks, 8 (53.3%) were women. The median age and BMI in oncologic patients was 73 years (72-74) and 25.6 kg/m^2 (22-29). In patients with a benign process median age was 37.5 years (23-61) and mean BMI 41.3 kg/m^2 (24-53); differences were not statistically significant probably because of our small sample size.

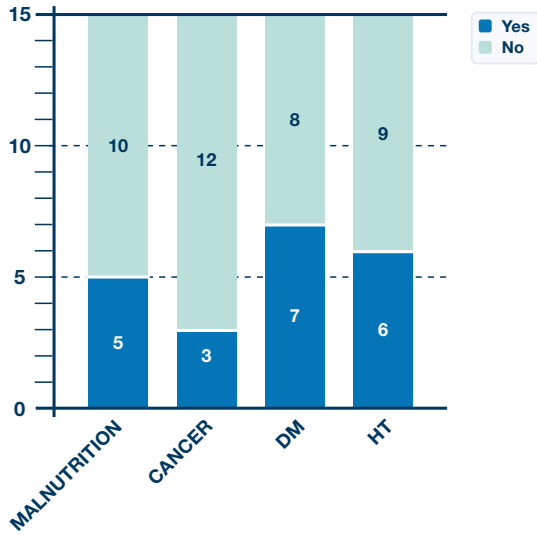

Figure 13: Associated comorbities in 15 patients with IAAL.

Most of the patients who developed leaks had multiple associated comorbidities *(figure 13)*, including hypertension (6), type 2 Diabetes Mellitus (7) and malnutrition (5). There were 4 with gastric cancer diagnosis, of whom 3 underwent neoadjuvant treatment. All of them presented preoperative proteins under normal levels. The differences between patients who developed leak or not are vitally important, but are not the prime concern in this particular study.

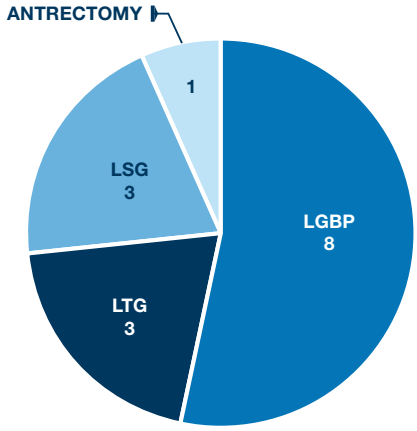

Figure 14: Previous surgery in patients diagnosed of IAAL.

Previous surgery *(figure 14)* in 8 (53.3%) patients was a LGBP, a LTG in 3 (20%), a LSG in 3 (20%) and in 1 (6.7%) open antrectomy with Roux-en Y reconstruction. First surgical procedure was performed in our center in 10 (66.7%) patients. Negative margins were achieved in 100% of the patients with a malign process.

3.2. CLINICAL AND DIAGNOSTIC CHARACTERISTICS

In our study there were no asymptomatic patients when diagnosis was achieved. Frequent clinical manifestations were *(figure 15)*: abdominal pain (13), tachycardia (11), tachypnea (10) *(figure 16)* and fever (6). The initial clinical status was in 5 patients mild sepsis, severe sepsis in 5, and septic shock in 2, being the only death of our series among this last group. Only 3 patients did not have SIRS criteria. During early postoperative, the presence of tachycardia with the absence of fever were important signs to exclude IAAL. In the same manner, discharge or change of secretion through the abdominal drain gave rise to the suspicion of leak *(figure 17)*: sero-hematic to purulent (5), intestinal (4), gastric (3), biliary (2) or saliva (2).

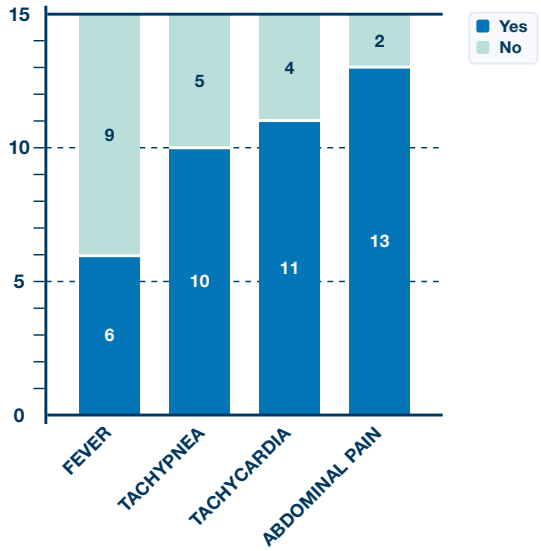

Figure 15: Clinical manifestations in patients diagnosed of IAAL.

Figure 16: Initial clinical status of septic shock was presented in 2 patient, one them deceased.

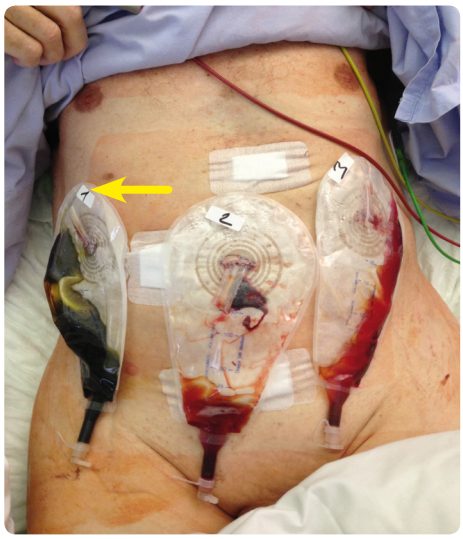

Figure 17: Suspicion of leak can be made also when a discharge or change of secretion through the abdominal drain occurs.

Table 7 shows the differences with regard to epidemiologic characteristics, symptoms and laboratory results between patients who underwent conservative or surgical treatment. Those who were diagnosed and operated afterwards had an increased presence of fever, tachycardia and tachypnea than patients who underwent conservative management ($p > 0.05$). Also levels of WBC count, CRP and PCT were higher ($p > 0.05$). Time of appearance after surgery and location of leak is shown too.

There were 10 patients diagnosed of acute IAAL and 5 cases of chronic leak. Seven patients developed anastomotic leaks at the GJA, one of them with an associated leak at the gastric remnant.

Table 7: Clinical characteristics, laboratory levels, time and location of IAAL in 15 patients with conservative or surgical management.

Clinical Characteristics	Total (n=15)	Conservative management (n=3)	Surgical management (n=12)
Age (years) median (SD)	44.6 (18.1)	44 (19.3)	44.8 (18.7)
BMI (kg/m²) median (SD)	38.2 (9)	40.7 (1.2)	37.6 (10)
Gender (female/male)	8F/7M	2F/1M	6F/6M
Fever (>38ºC)	6	1	5
Abdominal pain (VAS >6)	13	3	10
Tachycardia (>90 bpm)	11	2	9
Tachypnea (>20 bpm)	10	2	8
WBC count (mm³) mean (SD)	16,533 (2,875)	16,000 (1,732)	16,666 (3,143)
CRP (mg/dL) mean (SD)	162 (73.1)	133.3 (76.4)	169.2 (21.3)
PCT (g/L) mean (SD)	3.8 (2.2)	2.3 (1.5)	4.3 (2.2)
NO SIRS	3	1	2
Mild sepsis	5	1	4
Severe sepsis	5	1	4
Septic Shock	2	0	2
Time of appearance			
Acute IAAL	10	2	8
Chronic IAAL	5	1	4
IAAL location			
EJA	2	0	2
GJA	7	2	5
JJA	1	0	1
LSG stapler line	4	1	3
Duodenal stump stapler line	**1**	**0**	**1**

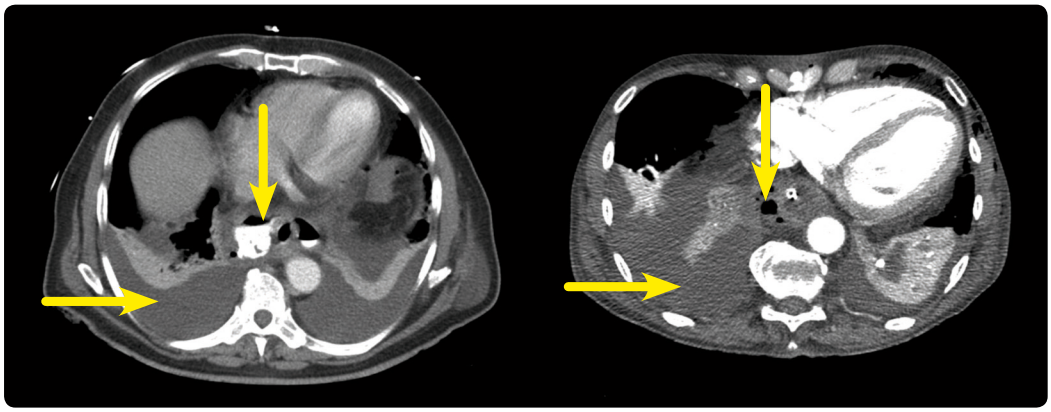

Figure 18: CT scan with oral and intravenous contrast showing IAAL findings: extravasation of contrast material through the anastomosis or a staple line, adjacent collection, free intra-abdominal liquid, pleural effusion and free intra-abdominal gas.

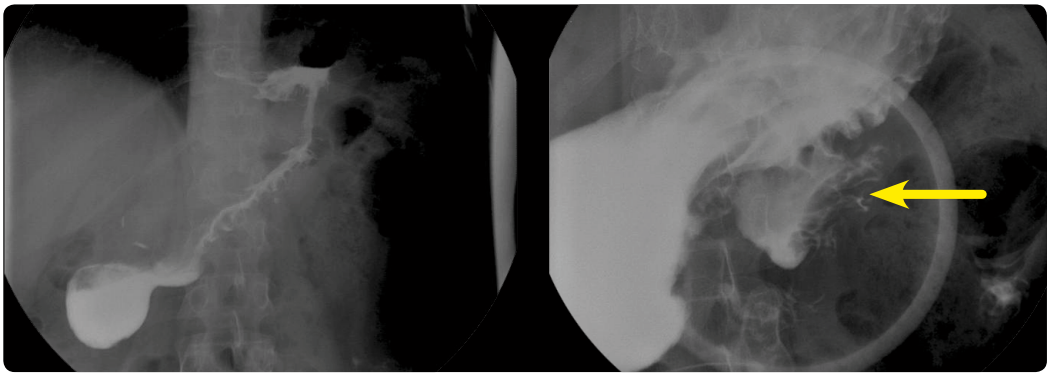

Figure 19: Transit with oral contrast can show-up chronic leaks with scarce clinical impact as well as they provide information about esophageal and gastric emptying.

IAAL diagnosis *(Table 8)* was achieved with a CT scan with oral contrast *(figure 18)* in 13 (86.7%) patients. Dehiscence was assessed by endoscopy in 9 (60%) patients, even before undergoing surgery in 5 of them, showing a leak in 7 patients and ischemic injury plus leak in 1 case. An anastomotic ulcer was described in 1 patient. Two (13.3%) patients were submitted to urgent exploratory laparoscopy because hemodynamic instability at diagnosis.

Table 8: Diagnostic methods of IAAL.

Anatomical IAAL Location	Clinical criteria	CT scan with oral contrast	CT scan+ preoperative endoscopy
EJA	0	2	0
GJA	1	4	2
JJA	0	1	0
LSG stapler line	0	1	3
Duodenal stump stapler line	1	0	0

3.3. MANAGEMENT DATA

Figure 20 : Patients' management resumed flowchart.

Due to patients' clinical status, radiological findings, leak localization and time of diagnosis of leak an immediate surgery was achieved in 7 patients. In the other 8, less invasive complementary exams were possible to perform (endoscopy, CT/US draining). Among these, conservatory management was applied in 4 of them.

3.3.1. SURGICAL MANAGEMENT

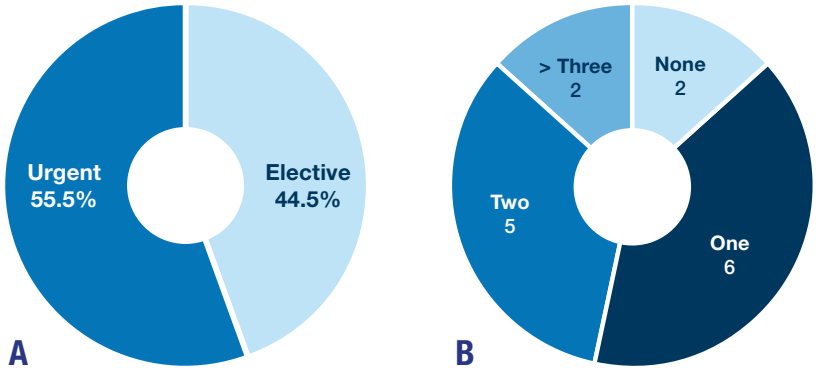

Figure 20: Characteristics of interventions in surgical management.
A: Urgent procedures were more common in surgical managment.
B: Number of reinterventions per patient treated with surgical management.

Surgical treatment was finally carried out in 11 (80%) patients. *Figure 15* show that reoperation was more frequently immediate and done once (40%). Laparoscopic approach was the most used (80%).

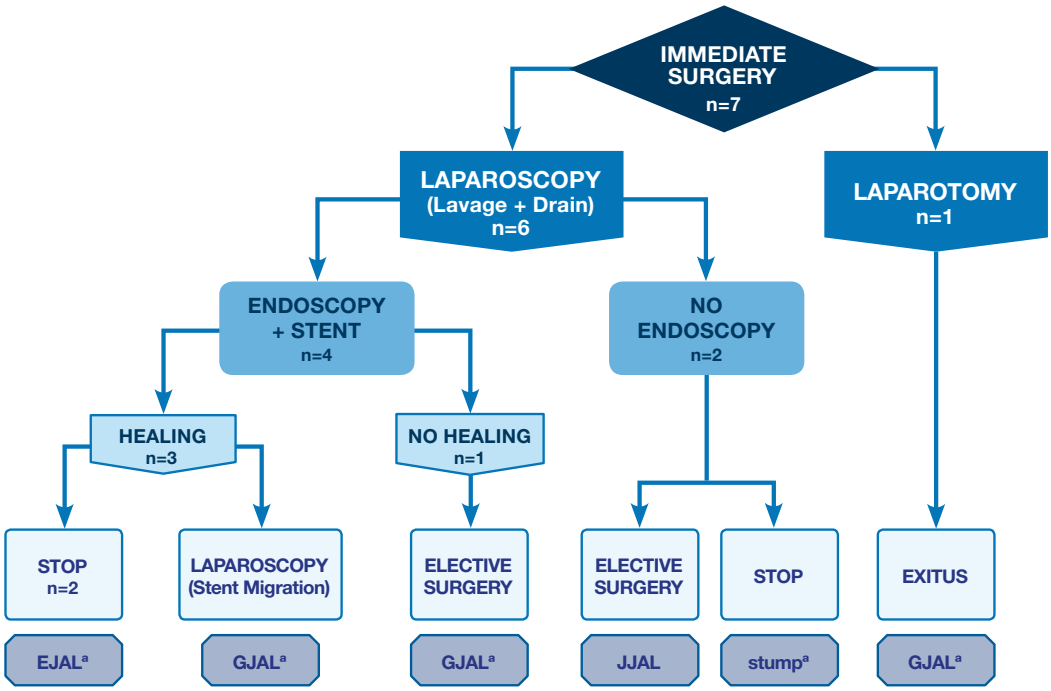

Figure 21 : Flowchart of patients who have undergone immediate surgery. [a] acute

Surgery was performed immediately in 7 patients (*figure 21*):

- 1 urgent laparotomy in a patient with an acute GJAL after LGBP.

  Patient died with a laparostomy after 2 days in ICU.

- 6 laparoscopies for peritoneal washout and effective drain placement.

  After intraoperatory findings, 2 patients were not candidates for endoscopical exploration:

  - An acute leak in the staple line of duodenal stump, that did not require further invasive treatments.
  - An acute JJAL that afterwards needed an elective surgery for resection and redo of JJ anastomosis *(figure 22)*.

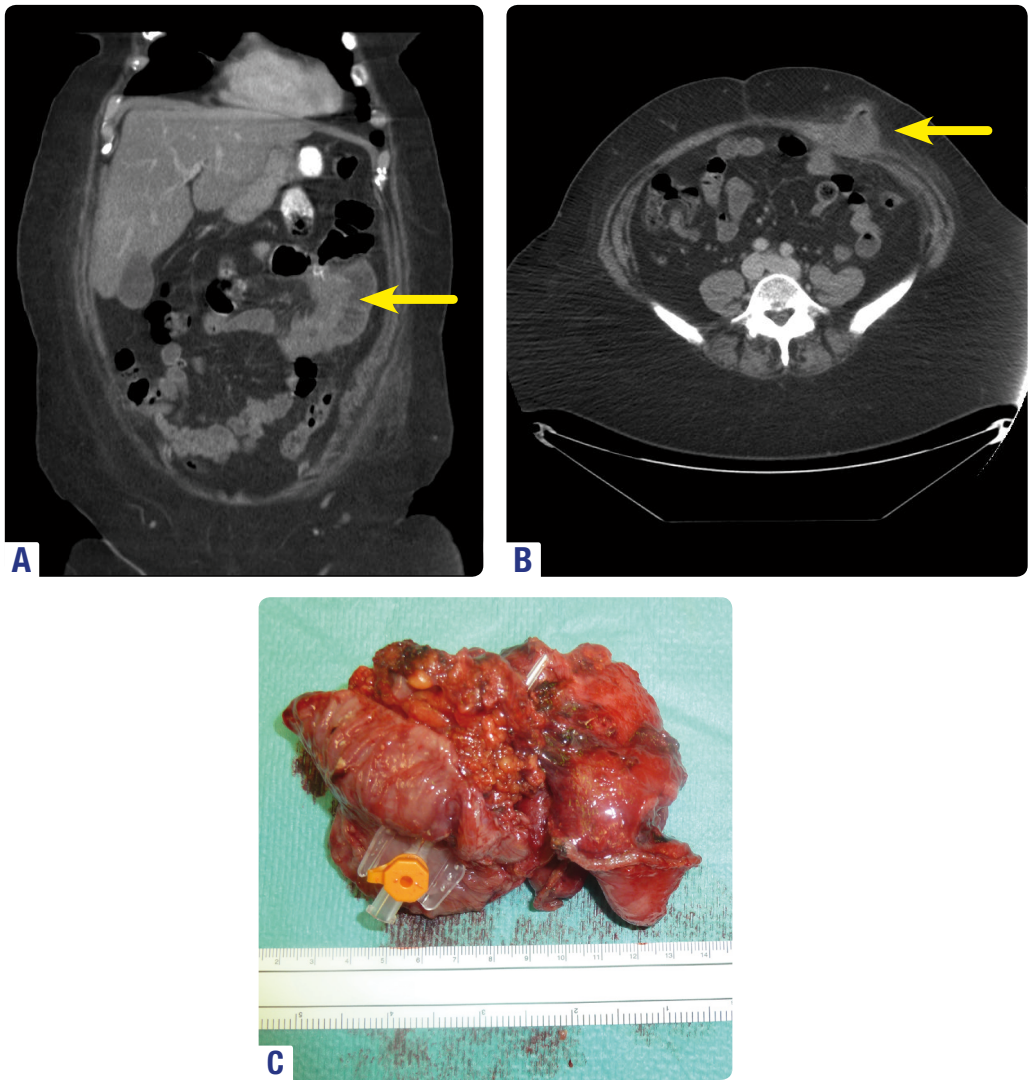

Figure 22 : A and **B**: Radiological findings of a JJAL with abscess in abdominal wall. **C**: Specimen of JJA anastomosis with leak orifice indicated with catheter.

Post-operative endoscopy and stent deployment was achieved in the other 4 patients *(figure 23)*. Healing of the leak was completed in 3 cases: 2 acute EJAL and 1 acute GJAL (which needed re-operation by laparoscopy due to stent migration). Sealing was not achieved after stent positioning in 1 patient, an acute GJAL after a LGBP, who required another 2 re-operations (1 laparotomy and 1 thoraco-phrenic laparotomy).

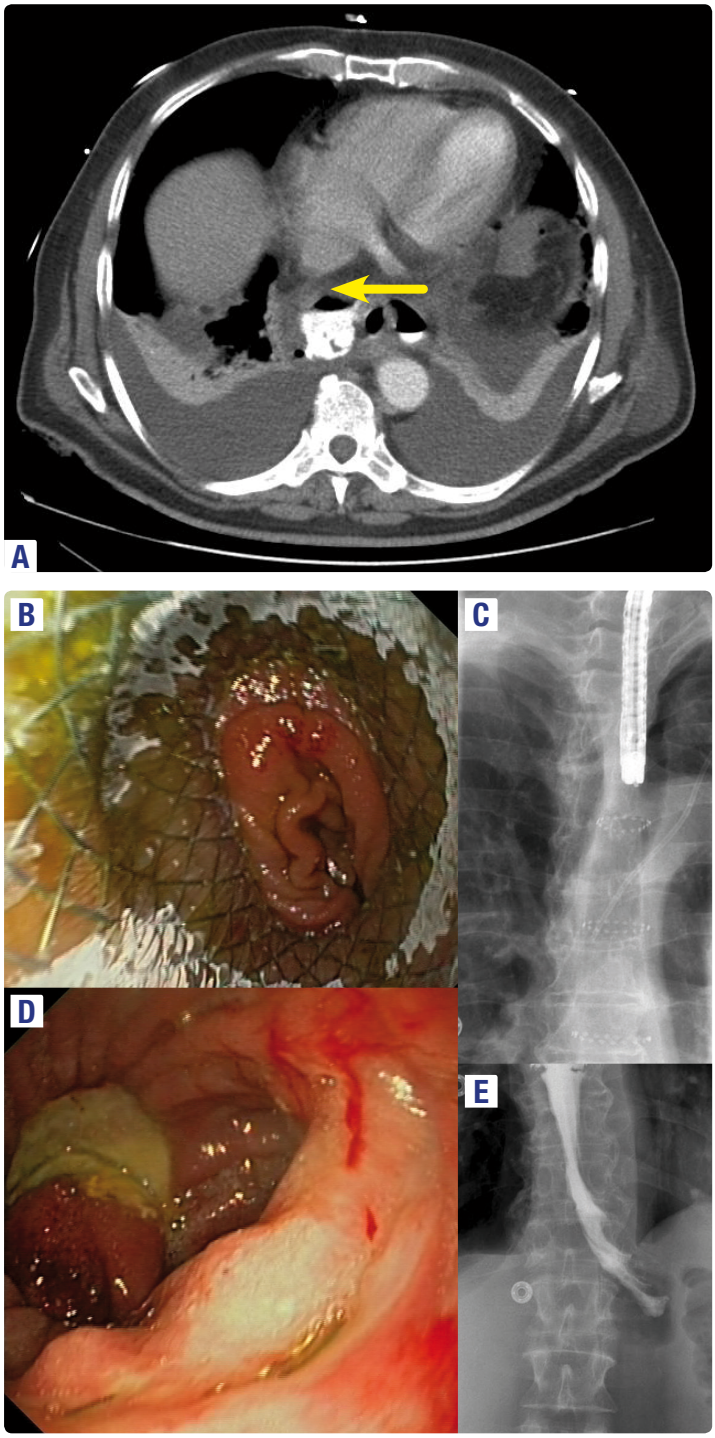

Figure 23 : A: CT scan showing an acute EJAL. **B,C**: Stent deployement and radiological control. **D,E**: Leak sealed after stent retrieval and transit with oral contrast without extravasation.

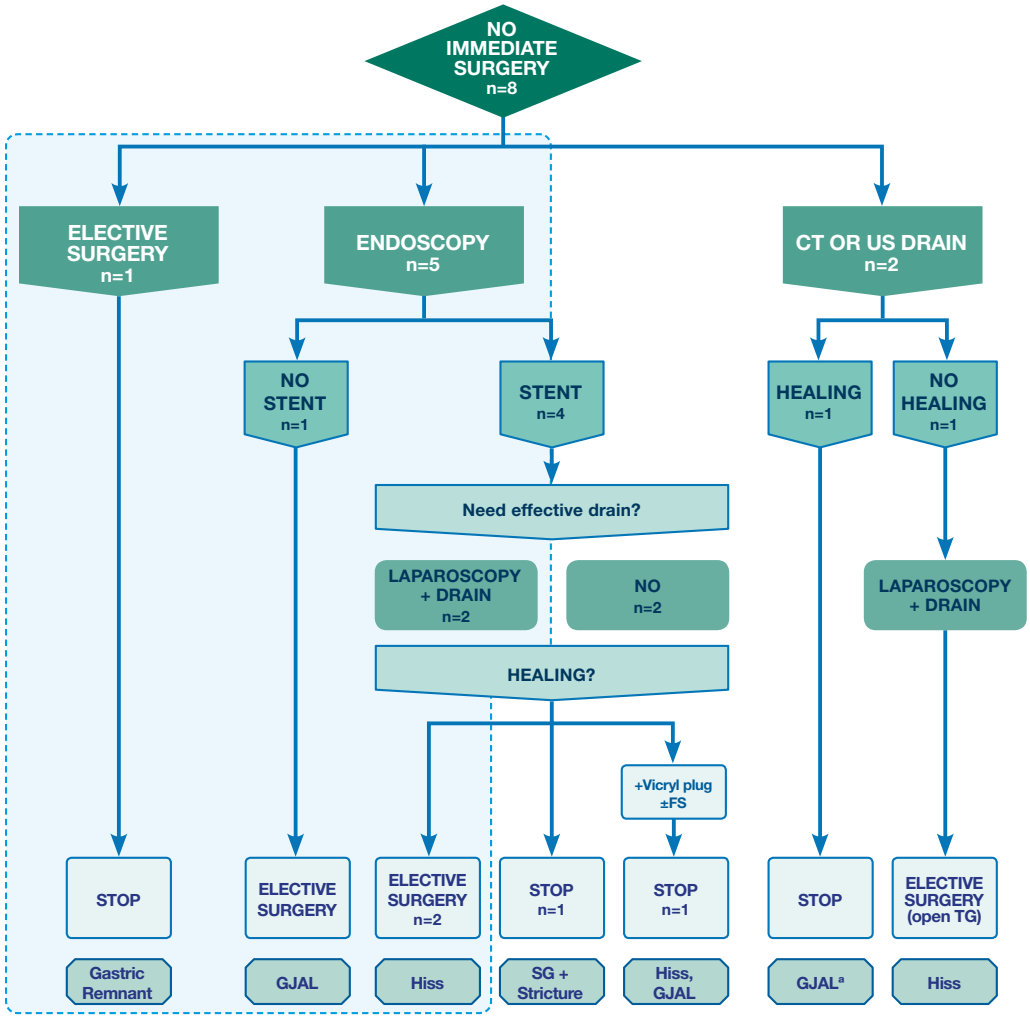

Figure 24: Flowchart of patients with no-immediate surgery. Shaded area represents those who finally required surgical management. **FS**: fibrin sealants.

Due to clinical status and/or radiological findings 8 patients did not go immediate surgery *(figure 24)*, allowing other exams to accurate their management and therefore, selecting patients candidates to conservative management (4).

A chronic leak from GJA to the gastric remnant, well tolerated, was candidate to elective surgery once the inflammatory process had been treated with antibiotics. A laparoscopic fistulectomy was performed and patient was discharged *(figure 25)*.

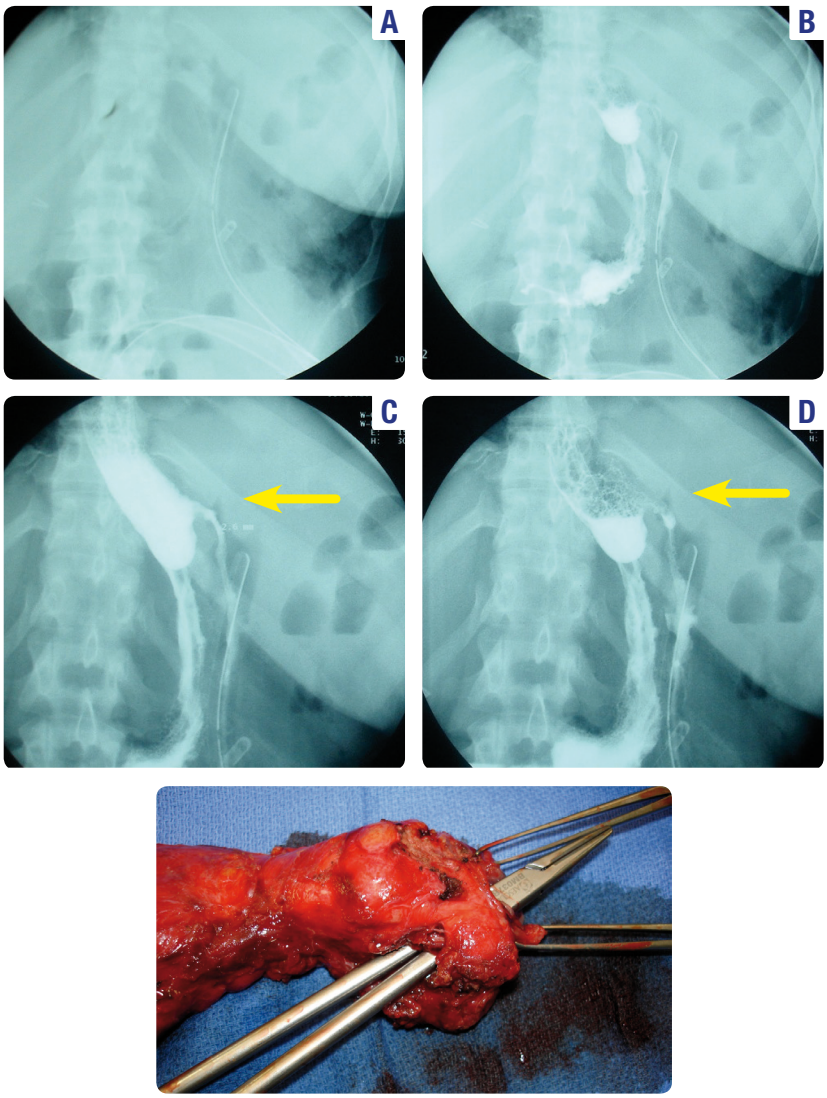

Figure 25: Chronic IAAL in Hiss angle after LSG. Healing was not carried out and an elective open total gastrectomy was performed.

Endoscopy was performed in 5 patients recognizing patients for either surgical (3) or conservative (2) treatment due to IAAL characteristics:

- Stent positioning followed by urgent laparoscopy for effective drain placement was achieved in 2 patients with chronic IAAL after LSG (Hiss angle and upper third of staple line). In these cases, healing was not carried out and elective surgery was needed performing an open TG and a laparoscopic side-to-side GJ bypass *(figure 26)* covering a large defect respectively. In this last case, as intraoperative finding, a stricture of the sleeve was associated.

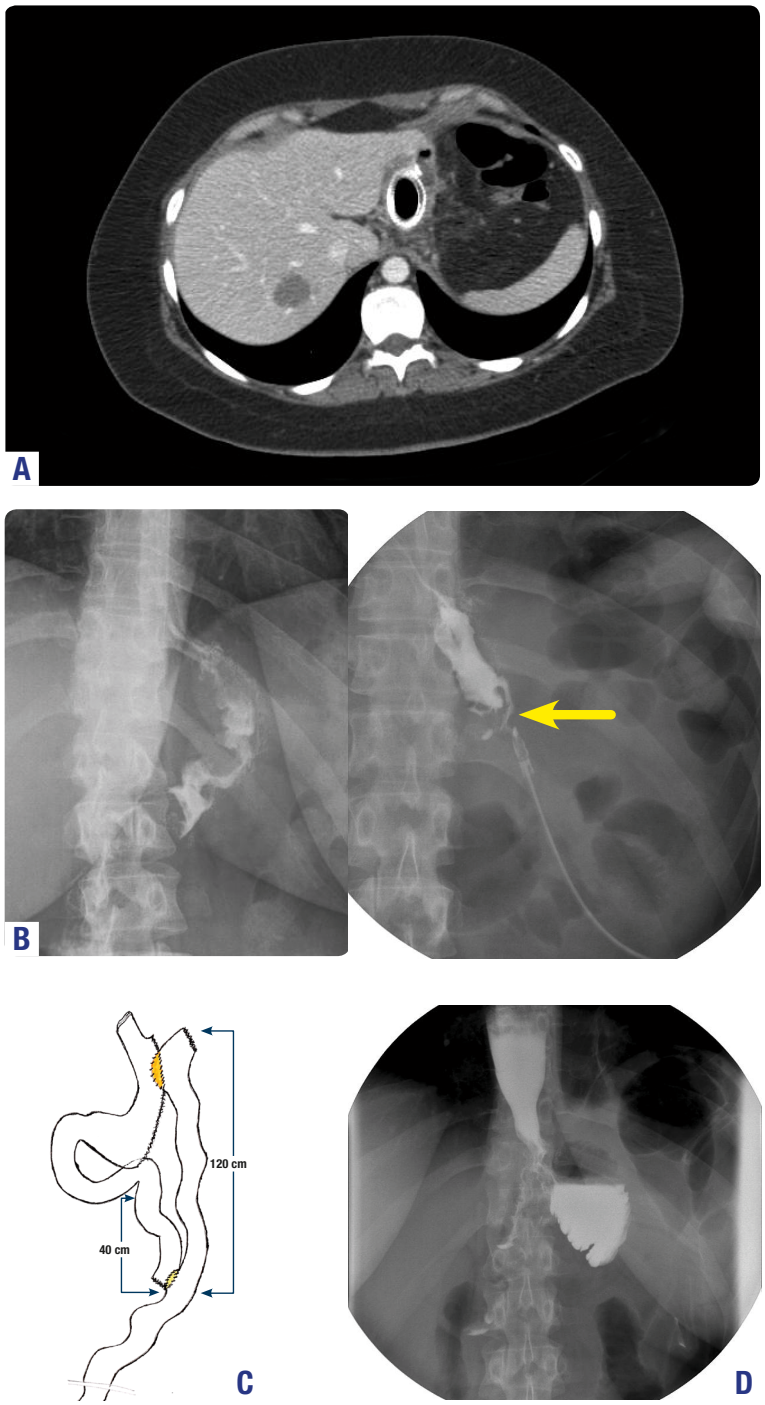

Figure 26 : Leak in upper third of staple line of LSG.

A: Initial conservative management with stent.
B: Transit with oral contrast after stent withdrawal showing a chronic leak.
C: Schematic drawing of the laparoscopic side-to-side GJ bypass performed.
D: Transit with oral contrast checking lateral GJ bypass.

- A chronic GJAL with an entero-cutaneous fistula after a Roux-en-Y antrectomy *(figure 27)* transferred from another center was not candidate for stent placement. After intravenous antibiotics, elective surgery was accomplished doing a laparoscopic Roux-en-Y degastro-gastrectomy. Insufficient gastric resection after a duodenal ulcer was found out to be the reason of this leak.

No procedure-related morbidity was observed in these patients where endoscopy was finally performed pre-operatory.

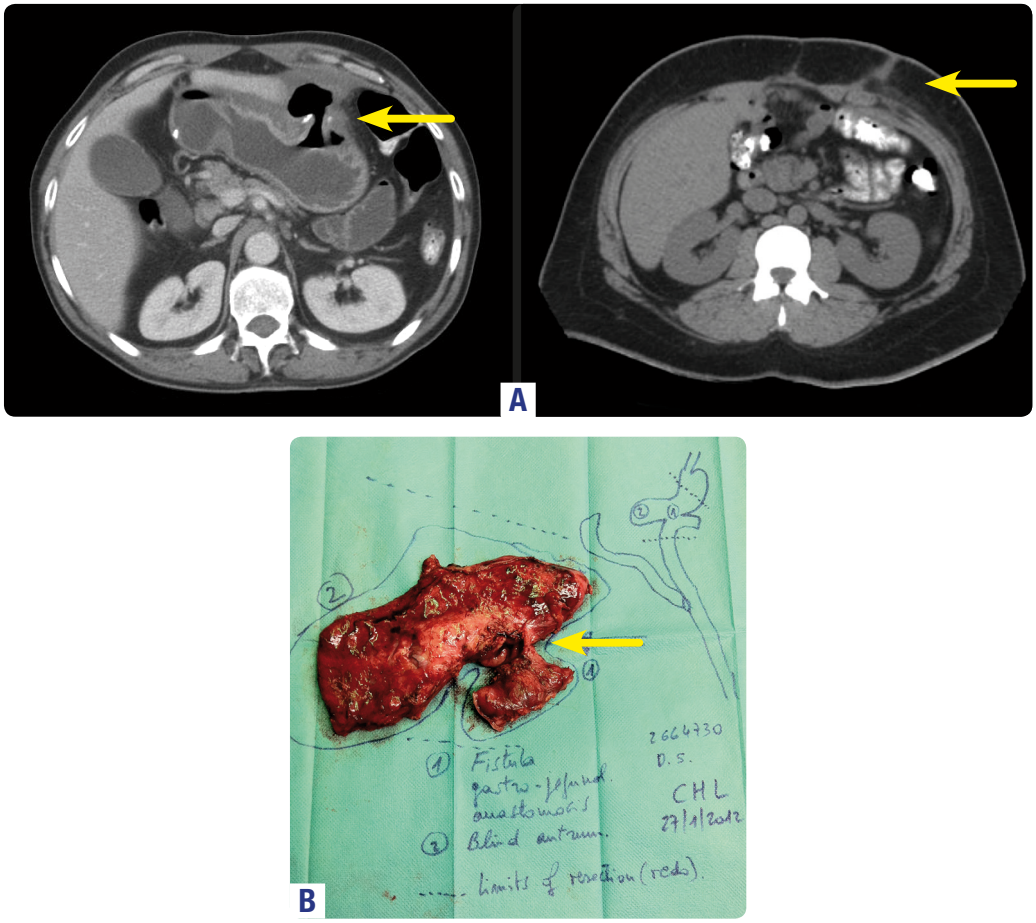

Figure 27 : A: Chronic GJAL with enterocutaneous fistule appears in CT scan with oral contrast. **B**: While definitive laparoscopic surgery, insufficient gastric resection after a duodenal ulcer was found out to be the reason for the leak.

3.3.2. CONSERVATIVE MANAGEMENT

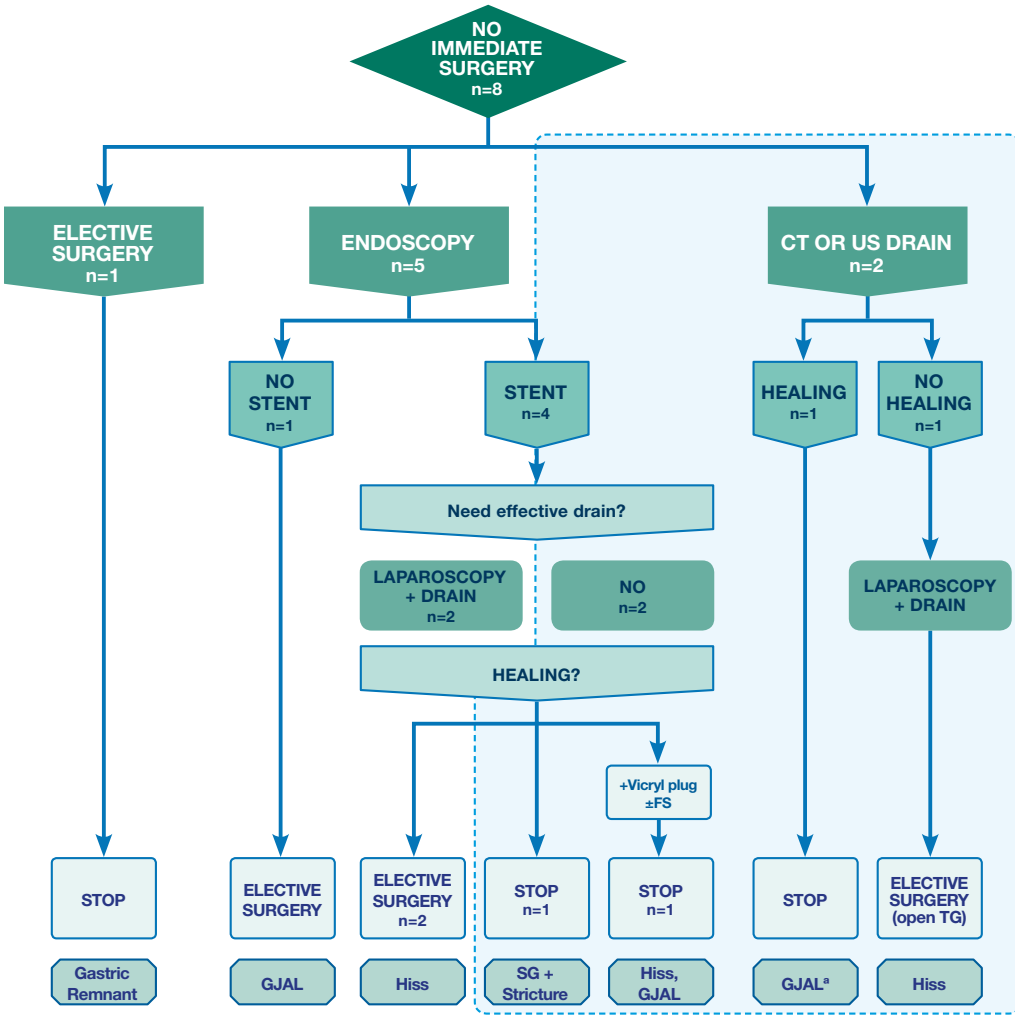

Figure 28 : Shaded area of flowchart highlights conservative management. [a] acute.

There were 4 patients, all of them with benign pathology, who underwent conservative management. They were hemodynamically stable and presented radiological findings like localized abscess and/or minimal perianastomotic oral contrast extravasation (if this liquid collection was more than 3 cm a percutaneous drain was placed). All of them were chronic IAAL, 2 in a GJA after LGBP and 2 in the staple line after LSG, next to GEJ.

In *figure 28* non-operative treatment is summarized. An effective percutaneous drain was required in 2 patients. In one case drain was effective and after 21 days, it was removed and patient was discharged. In only one case percutneous drain was not effective and patient has been managed surgically. It was a chronic IAAL in Hiss angle after a LGBP. A laparoscopy for effective drainage and peritoneal washout allowed optimal conditions to perform later an elective open total gastrectomy.

Other 2 patients underwent digestive endoscopy and stent was deployed. Treatment was completed with a percutaneous drain in 2 of them. The other patient suffered disphagia and stent was withdrawn. Treatment continued with endoscopic clips and fibrin sealants, without results. It is why 2 vicryl plugs were placed *(figure 29)* with 7 days delay between both of them. No leaks were seen in radiology series and healing was confirmed 4 weeks later.

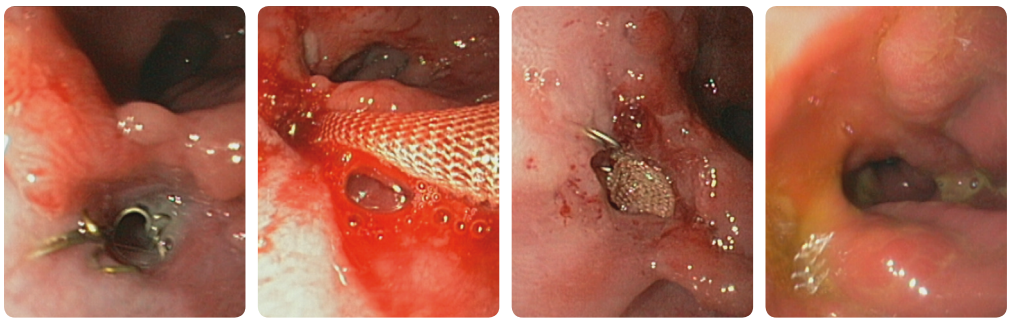

Figure 29: Other endoscopical treatments must be considered if there is no sealing with stent. Vicryl plug can achieve it.

Complications after conservative management are summarized in *table 9* further on. Conservative management healed leak completely in 3 out of 4 patients. Mortality rate was 0 in this group.

3.3.3. ENDOSCOPICAL TREATMENT

To summarize 8 SEMs were successfully placed in all patients. Mean healing time (time to stent retrieval) was 6 weeks. Leak occlusion was obtained in 5 patients (healing rate: 62.5%). Supplementary endoscopical treatments were used in 3 patients: clips and fibrin sealants carried trough healing in 2, and in the third case FS did not work; a vicryl plug was placed twice (with 7 days of difference) verifying sealing 7 days after.

Only 1 patient presented dysphagia; it was easily treated by stent removal. Migration of the stent was observed in 2 patients (migration rate: 25%). One stent was removed by flexible endoscopy and replaced; the other case developed bowel obstruction because of migration into the small intestine *(figure 30)* with subsequent failure to pass the stent through the rectum. The patient required an urgent laparoscopic reintervention for removal. No patients developed a stricture on the anastomosis.

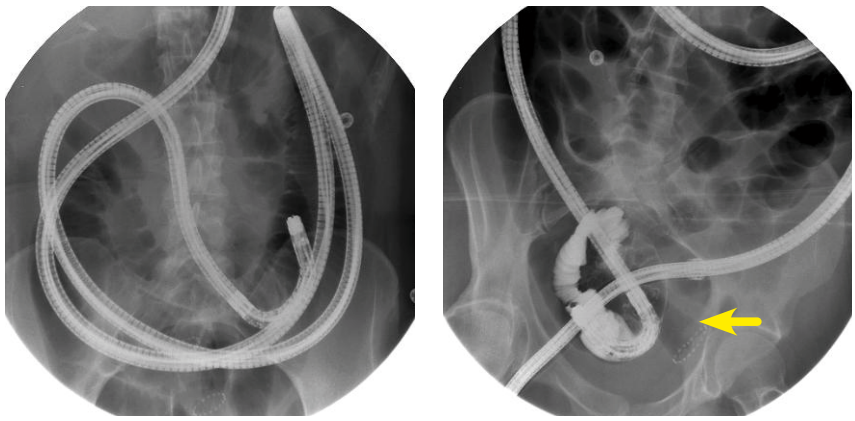

Figure 30 : Migration is an important drawback of stents, specially if it reaches small bowel. If withdrawal is not possible with endoscopy, laparoscopic retrieval is needed, accomplishing an enterotomy.

3.3.4. COMPLICATIONS

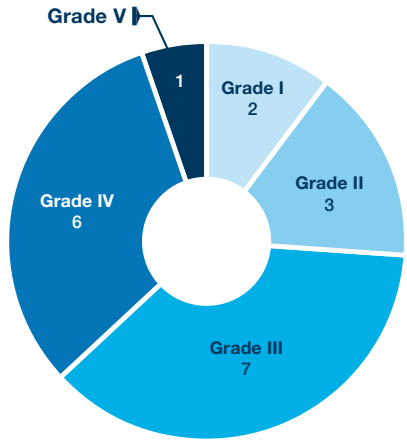

Figure 31: Complications in 15 patients with IAAL according to Clavien-Dindo classification.

Complication rates and a comparison between patients who underwent conservative versus surgical treatment are summarized in *figure 31* and *table 9*. The most frequent complications (38.8%) were

those that required surgical, endoscopical or radiological intervention (Clavien-Dindo III). Life-threatening complications requiring ICU management (Clavien-Dindo IV) were 33.3%. These major complications (ARDS, MOF,) were more common in patients who underwent surgical treatment (5) versus conservative treatment (1) ($p > 0.05$).

Table 9: Comparison of hospitalization and operative complications between patients with IAAL managed conservative versus surgical. **UTI**: urinary tract infection - **IAA**: intraabdominal abscess - **RF**: renal failure **ARDS**: acute respiratory syndrome - **DIC**: disseminated intravascular coagulation - **MOF**: multiorganic failure

Characteristics	Total (n=15)	Non-Operative (n=3)	Operative (n=12)
Transfer from other centers	5	1	4
Readmission	8	3	5
Median length of ICU stay after treatment in days (SD)	12.8 (19.5)	10	13.1 (20.7)
Median length of hospital stay after diagnosis in days (SD)	21.5 (23.5)	15 (6.5)	23.1 (26.2)
Median length of global hospital stay in days (SD)	23.7 (23.5)	15 (6.5)	26.1 (26.2)
Complications			
Grade Clavien-Dindo I	2 (11.1%)	1	1 wound infection
Grade Clavien-Dindo II	3 (16.6%)	1	2 UTI
Grade Clavien-Dindo III	7 (38.8%)		
IIIa		1 disphagia	4 tracheotomy, eschar, IAA, pleural effusion
IIIb			2
Grade Clavien-Dindo IV	6 (33.3%)		
IVa		1 RF	3 ARDS, DIC
IVb			2 MOF
Mortality n (%)	1 (6.6%)		1

It is to be noted that in non-operative management group a minor complication due to stent (dysphagia) was present in 1 patient. Only 1 patient developed a major complication (renal failure) that required ICU admission.

On the other hand, in the surgical management group, 5 major complications were registered. Four patients developed various combinations of respiratory, congestive and renal failure, and intraabdominal abscess or eschars with different degrees of severity. Patients with conservative management had short intensive care course (mean: 10 days versus 13 days) and hospital stay (mean: 15 days versus 26 days). Statistical analysis by subgroups revealed that male gender with malignancy had longer stay; there was no significance probably due to the small sample size. Mortality was not observed after

conservative treatment and/or stent insertion, whereas 1 patient died from septic complications and multiorganic failure after surgery (in-hospital mortality rate 0% versus 6.6%).

discussion

Anastomotic leaks are a serious complication in patients undergoing UGI surgery for contributing significantly to operative morbidity and mortality independent of underlying comorbidities.[72] It also affects long-term survival, quality of life and prolongs hospital stay as well as increases costs of therapy.[12,22] In the setting of a leakage in an oncologic patient, growth of residual tumor cells may be affected by the increased magnitude and duration of inflammatory response [73] determining this event as an independent predictive factor for overall survival. Also physical deterioration and a weakened immune system makes these patients no longer candidates for adjuvant treatment.[12,73] Moreover patients with a IAAL have a higher incidence of wound infections, sepsis, thrombo-embolic events, internal hernias, small-bowel obstruction, and respiratory and renal failure.[26] Therefore IAAL management remains a challenge. Considering that bariatric procedures are constantly increasing, we have to expect a rise in postoperative complications, anastomotic leakage among them. Besides the clinical impact this implies an increase cost of the treatment. Consequently nowadays we think it should be considered like a real public health problem.

4.1. IAAL DEFINITION AND INCIDENCE

These days the most frequent UGI procedures holding an anastomosis and its potential complications are: subtotal and total gastrectomy, gastric bypass and sleeve gastrectomy. Considering that intratorathic anastomosis of esophageal surgery are localized in another cavity and may differ in their treatment, it has been excluded of this study. Therefore we propose defining intraabdominal anastomotic leak after UGI surgery as a defect of the intestinal wall at the anastomotic site (including suture and staple lines of section margins) of EJA, GJA, JJA and staple line leaks, leading to a communication between the intra- and extra-luminal compartments. As several authors suggested,[74–78] they may be considered also peri-anastomotic abscess even if no communication can be proven with the intestinal lumen at the anastomosis.

Table 10: Incidence of gastrectomy for cancer leak.

Group	Year	Reconstruction	n	Leak (%)
Roder [79]	1993	No specified	1654	7.2 - 12.7
Bonenkamp [80]	1995	No specified	1078	9
Lang [40]	2000	Roux-en-Y EJA	1114	7.5
Portanova [81]	2010	Roux-en-Y EJA	173	5.2
Sah [20]	2010	Multiple	1559	2
Sierzega [12]	2010	Roux-en-Y EJA	690	5.9
Bracale [82]	2010	Side-to-side	67	6
Yoo [73]	2011	Roux-en-Y EJA	478	2.9
Lim [83]	2012	Roux-en-Y EJA Billroth I and II	393	2.2
Migita [10]	2012	Roux-en-Y EJA	327	5.8
Deguchi [27]	2012	Roux-en-Y EJA	1640	2.1
CHL	2013	Multiple	121	3.3

Bearing in mind that IAAL definition after UGI surgery has not been considered yet in literature, comparing our IAAL rate with other studies is not possible, hence it will be compared by surgical procedures. Leakage rate in gastrectomy for cancer in our study was 3.3%. Compared to international series *(table 10)* our rate is among the lowest. Nevertheless it is important to note that leakage rate is independent of the type of reconstruction and surgical radicality.[40] Leak rate after LGBP *(table 11)* in our group was 0.48%, also between the lowest. The incidence of LSG leaks *(table 12)* ranges between 0 and 7%, since our 3.7% rate is among the lower incidence. It should be noted that this table includes series with super-obese patients (BMI>50 kg/m^2) where leak rates are significantly higher.

Table 11: Incidence of LGBP anastomotic leak.

Group	Year	N	Leak (%)
Higa [84]	2000	1040	1
Marshall [85]	2003	400	5.2
Podnos [86]	2003	577 2497	1.73 1.98
Papasavas [87]	2003	246	1.6
Dresel [88]	2004	120	0.01
Fernández [89]	2004	3000	3.2
Suter [91]	2006	466	1.9
Durak [90]	2008	1133	1.5
Maher [92]	2008	450	2
Thodiyil [93]	2008	2675	1.7
Ballesta [15]	2008	1200	4.9
Csendes [50]	2012	1764	3.4
CHL	2013	1654	0.48

Table 12: Incidence of LSG anastomotic leak.

Group	Year	N	Leak (%)
Johnston [94]	2003	100	1
Moon [95]	2005	130	1
Cottam [96]	2006	126	2
Lalor [97]	2007	148	1
Lee [98]	2007	216	1
Nocca [99]	2007	163	6
Weiner [100]	2007	120	3
Felberbauer [101]	2007	126	0
Rubin [102]	2008	120	0
Skrekas [103]	2008	93	4
Burgos [104]	2009	214	3
Fuks [105]	2009	135	5
Menenakos [106]	2009	261	4
Sanchez [107]	2009	540	2
Casella [108]	2009	200	3
Stroh [109]	2009	144	7
Armstrong [110]	2010	185	0
Csendes [111]	2010	343	5
Lacy [112]	2010	294	4
Ser [113]	2010	118	3
Srinivasa [114]	2010	253	2
Bellanger [115]	2011	529	0
CHL	2013	81	3.7

After an exhaustive literature review we can conclude that a universally accepted definition of anastomotic leakage of UGI surgery is needed, as well as common agreed standardized diagnostic algorithms and uniform grading of severity. This may also contribute to have uniform criteria that would facilitate valid comparison of the results of different studies improving its management.

4.2. DIAGNOSIS

Because epidural analgesia and laparoscopy diminish postoperatory pain, clinical signs and symptoms are mitigated; therefore a high index of suspicion should be maintained. We know there are patients with a higher risk to develop this complication and we have criteria to detect them. Also, identification of patients with severe sepsis or septic shock is carried out thanks to SIRS classification, an easy, effective, universal and low-cost method that can be performed bedside. Noteworthy is the absence of studies that correlates SIRS classification system with IAAL suspicion as well as the need of the diagnostic of the anastomosis' morphologic characteristics. Early diagnosis of leakage will allow a prompt

and adequate management in a patient with no organ failure, but nevertheless radiological exams should not delay urgent surgery with the exception of a clinical context of pulmonary embolism.[116]

Lamb et al [117] in 2004 conclude "that there is no role for routine contrast swallow after total gastrectomy with a mechanical EJA, but patients with clinical suspicion of leakage should undergo urgent contrast radiology, plus endoscopy if the contrast examination is normal". In bariatric surgery, a systematic esophagogram with oral contrast does not improve early diagnosis of leakage because of a high false negative rate (70%).[28] The reason why, is that many leakages occur immediately after the exam is concluded. [28] The great value of this exam is when it is performed in patients with clinical suspicion, where it can achieve a sensitivity up to 92%.[2] In addition, a CRP determination during 2 POD is a great value to predict postoperative complications, especially anastomotic leaks. Warschkow et al [118] propose that radiological exams could be restricted to those who present CPR levels above 229mg/l. It is to note that CRP can present elevated levels until 5th POD.[119]

Today thorax-abdominal CT scan with oral contrast and/or intravenous contrast can demonstrate extravasation of contrast material through the anastomosis or a staple line, an adjacent collection, free intra-abdominal liquid, oral contrast material residue in the drainage tube, pleural effusion and/or free intra-abdominal gas.[120] But important limitations exist in its accuracy, in part because of issues inherent to the bariatric patient population that could make CT imaging impractical or impossible.[121] When UGI studies and CT are combined, up to one third of patients will have both studies interpreted as normal, despite the presence of a leak, so endoscopical or/and operative exploration [32] should be considered part of the diagnostic algorithm. It also may be borne in mind that surgical re-exploration that reveals no explanation for a post-operative patient's worrisome clinical findings or deterioration should be considered an appropriate and indicated intervention and not a complication.[121]

Classically, endoscopy has been contraindicated in patients with anastomotic leak because it was thought that it could aggravate due to irritation and air insufflation. Page et al [122] valuated the safety and efficacy of endoscopy in diagnosing anastomotic leaks in 100 consecutive post-esophagectomy patients, all having reconstruction using the stomach. Endoscopy was performed within the first

week after operation. There was no evidence that the procedure caused damage to the anastomosis or gastric conduit. Endoscopic exploration is a safe and highly accurate method of diagnosing leaks [45] providing unique information on the condition of the anastomosis allowing a more targeted approach to patient care in the context of anastomotic healing and in the treatment of leaks. To conclude, it is useful diagnosing leaks that are not seen in CT scan or esophagogram.[23]

In our study there was no evidence post-operative that endoscopy caused damage to the anastomosis or gastric conduit. Seven (46%) patients who underwent pre-operatory endoscopy did not show differences in both reintervention or post-operative complications with respect to the others and…, and no further leaks developed subsequently, making endoscopy 100% accurate in the diagnosis of leaks after UGI procedures and providing useful information to plan a better surgical technique during re-operation. Thence until a few years ago in our center, when hemodinamically stable patients had torpid evolution or clinical suspicion a CT scan was performed; nowadays endoscopy is our first diagnostic method.

4.3. TREATMENT

Treatment of IAAL has to be multidisciplinary, established promptly and determined by hemodynamic conditions of the patient and the characteristics of leakage to assure enteral nutrition as soon as possible. Enteral feeding started early during the treatment plays a significant role in leak closure.[123]

When proposing management, it is particularly important to considerate the severity, the location of the leak and the day of appearance. As Csendes et al [50] resume: in early leaks after surgery, with abdominal or pleural diffusion in CT scan and severe clinical and septic manifestations, localized in GJA or JJA, prompt surgical repair is needed. On the contrary, if leak appears several days after surgery, in the gastric remnant or in GJA, even if they have same CT scan findings, conservative management can be achieved.

However, some authors stand that surgery remains the mainstay of treatment for leaks in bariatric procedures.[72] Ballesta et al [15] reported that 39% of patients with leak required surgery. Carucci et al [124] founded that 81% of patients required a revisional bariatric procedure. On the other hand, we must not forget that this procedure carries a higher complication rate because of added technical difficulty and patient comorbidity.[72]

4.3.1. SURGICAL MANAGEMENT

Hemodynamic unstable patients with severe sepsis, abdominal or pleural diffusion in CT scan need a prompt surgical repair.[2,50] Laparoscopic approach is performed in our center when status of the patient allows it. Thus, the role for laparotomy remains anecdotal for hemodynamic unstable patients excluded of mini-invasive treatment, in order to diminish disadvantages and complications of operative treatment. Among these are included infection, dehiscence and eventration of the wound, complications originated from the alimentary jejunostomy and intraabdominal compartment syndrome.[2]

It is to mention the important role of laparoscopy, which provides a good evaluation of the status of the anastomosis (tissue perfusion, ischemia, size), consents a peritoneal lavage and positioning effective drains around the anastomosis. If needed, it also consents placing an alimentary jejunostomy. It is to be noted the particular benefit of this technique for leaks located in EG union, where placement of a percutaneous drain is particularly difficult. Reintervention has to be done very carefully avoiding tractions that can enlarge the defect. Primary repair in GJA, EJA and JJA is usually difficult due to the dense inflammatory infiltration and deep edema around the anastomosis.[49,125–127] Thereby, except in the rare cases in which the defect can be easily identified and the tissue in the area is viable, primary repair should be referred.[128] In these cases, wide drainage of the diaphragmatic space is the best option.[85] Usually, within days, a reactive pleural effusion appears and systematic drains are not required.[129]

Also patients who fail medical therapy or who may not be candidates for medical therapy alone may go on to experience the development of persistent leaks that will require surgical revision.[72] Reoperation in leaks after LSG should be the exception and not the rule.[129] Recent studies *(table 13)* have demonstrated that non-operative treatment (percutaneous drainage, endoscopy, stent) is feasible, safe and effective; furthermore, it may avoid more mutilating procedures such as total gastrectomy.[108] In our study, 2 out of 3 LSG did not accomplish the goal with conservative treatment and underwent elective surgery. In one case, it was due to persistence of the fistula after stent, clips and fibrin sealants; an elective open TG was performed. In the other case, conservative treatment did not work out because leak was associated to stricture of the neo-gastric tube. In this case a lateral

bypass was achieved with a jejunum loop. Nevertheless, with stent placement, leak became chronic allowing definitive surgery when patient has been optimized clinically and nutritionally.

4.3.2. CONSERVATIVE MANAGEMENT

Hemodynamic stable patients, asymptomatic or with optimal clinical tolerance to leak (usually chronic IAAL) and no severe sepsis symptoms are candidates to multidisciplinary conservative management. The mainstay of this treatment is intravenous antibiotics, an effective drain and adequate nutritional support. To avoid additional morbidity and mortality associated with reoperation,[61] several authors have described the use of endoscopically placed self-expandable stents in the management of post-operative leaks. Formerly results where published by surgical procedures however, as *table 13* shows, trend has changed and UGI post-operative leaks results are being published.

Once the effective drain (surgical or radiological) and optimization of general status of the patient are made, healing of the leak is achieved with a stent, which provides a physical barrier between the leak and the luminal contents, allowing the leak to heal while providing enteral nutrition, preventing parenteral nutrition disadvantages (cost, risk of vascular thrombosis and sepsis, less efficacy than enteral nutrition).[2] Other advantages are, when necessary, that endoscopy enables collection drainage or placement of a naso-jejunal tube.[81,123] Stent can be placed when anastomosis has signs of good perfusion [45] and a circumference defect is less than 70%.[38,48,144] When possible, it can be deployed at the same time exploratory laparoscopy is performed, and whenever operative time and ICU resuscitation are not delayed.[129]

Literature analysis revealed there is a lack of randomized controlled trials and that clinical success *(table 13)* of stent placement was achieved in almost 79% of reported patients with no differences between PSEMS and SEPS. The mean time of stent placement that was needed for healing was 5.3 weeks and was not different between different stent types (range 3–10 weeks). Animal studies have suggested that 4 weeks should be sufficient for tissue healing.[46] Based on the results of this study, however, it seems advisable to remove stents after a period of approximately 6 weeks because a shorter interval leads to incomplete leak closure and a longer interval may lead to stent migration or mucosal hypertrophy with increased difficulty of stent extraction or subsequent dysphagia.[72]

Table 13: Quantitative analysis of literature review with all available studies on stent theraphy that compromised 10 or more patients with esophageal anastomotic leakage after esophaguectomy, bariatric surgery or UGI surgery. **CR**: Case Report - **Retros**: Retrospective - **P**: Prospective - **SReview**: Systematic Review.

Procedure	Group	Year	Study Type	n	Stent Type	Sealing Rate (%)	1st Attempt Success Rate (%)	Migration Rate (%)	Removal Time (Average)	Mortality Rate (%)
ESOPHAGUECTOMY										
	Doniec [41]	2003	CR Retros	21	SEMS	81	Not reported	5	?	5
	Hünerbein [130]	2004	CR	9	SEPS	88	Not reported	22	4w	Stent-0 Surgery-20
	Schubert [44]	2005	CR	12	SEMS	92	100	16	2-8w	Not reported
	Kauer [131]	2008	CR	10	SEMS	70	Not reported	40	6w	Not reported
	Dai [61]	2009	CR	22	SEPS	91	41	23	6w	4.5
	Schweigert [132]	2011	CR	12	SEMS	83	Not reported	Not reported	Not reported	17
	Freeman [133]	2011	CR	17	SEMS/ SEPS	94	18	82	17-9d	Not reported
BARIATRIC SURGERY										
	Salinas [52]	2006	CR	17	SEMS	94	100	6	2-4m	?
	Eisendrath [134]	2007	CR	21	SEMS	81	62	5	Not reported	Not reported
	Eubanks [135]	2008	CR	13	SEMS/ SEPS	85	Not reported	58	6w	0
	Iqbal [136]	2010	CR Retros	19	SEMS/ SEPS	85	46	47	4w	0
	Begé [137]	2011	P	22	SEMS		Not reported	59	Not reported	0
	Puli [72]	2012	SReview	67	SEMS/ SEPS	88	Not reported	17	13d-7m	0
	Simon [138]	2013	CR	9	SEMS	78	Not reported	0	6w	Not reported
UPPER GI SURGERY										
	Siersema [42]	2003	CR Retros	11	SEMS	82	Not reported	9	7w	Not reported
	Langer [43]	2005	P	24	SEPS	92	Not reported	41	Not reported	25
	Tuebergen [125]	2008	CR	32	SEPS	78	50	6	46d (4-426)	15.6
	Salminen [139]	2009	CR	10	SEMS	80	70	10	5w	30
	Leers [39]	2009	CR	31	SEMS	92	84	3	6w	Not reported
	Blackmon [140]	2010	P	23	SEMS	61	26	43	1m	16
	Dai [143]	2011	CR	41	SEPS/ SEMS	86	7	35	23d	2.4
	Feith [45]	2011	CR	115	SEMS	70	Not reported	53	54d	9
	Swinnen [47]	2011	CR	88	SEMS	78	Not reported	14	8-10w	Not reported
	D'Cunha [141]	2011	CR	37	SEMS/ SEPS	60	16	Not reported	33d	18.1
	van Boeckel [38]	2011	SReview	267	SEMS/ SEPS	85	Not reported	12 -31	7w	13
	van Boeckel [46]	2012	CR	52	SEMS/ SEPS	76	99	19	25d	2
	Donatelli [123]	2013	CR	15	SEMS	93	Not reported	33	28-73d	Not reported
	Yimcharoen [142]	2013	CR	18	SEMS/ SEPS	72	Not reported	22	Not reported	11
	CHL	2013	CR	8	SEMS	62.5	8	25	6w	0

With regard to our study, our number of patients treated with stent is low, but it is to remark that our global leak rate is very low. Like most of the other series, this study is a retrospective cohort and SEMS are placed. Our success rate (62.5%) is below the average rate but this is influenced by our small sample size. The majority of leaks managed with stent resolved on the first attempt. Time stent was placed (6 weeks), was among the average rate of the studies (5.7 weeks (range 3.5-10)).

The main drawbacks are stent migration and tissue in or over-growth. Complication rate due to stents varies between 23-29% in the main series; rates are higher treating EGJ anastomotic leaks.[123] Minor complications include transient dysphagia/nausea/vomiting, dysphagia caused by severe hyperplasia, distal ulcers and rupture of coating in SEMS. They can be easily treated by SEMS removal, balloon dilation or SEPS insertion.[47] Major complications (bleeding, tracheal compression and perforation) are rare and are related to specific conditions such as an anastomotic leak with tight angling.[47] Strictures in the place of mucosal hyperplasia are the main long-term complication after SEMS removal. It can be treated with balloon dilation.[47,145]

The high migration rate is likely related to the design of the stents rather than the endoscopist's technique.[72] It is also significally lower in nititol stents, superposed stents, polyester stents larger than 15 cm and nititol stents larger than 12cm.[136] Several authors have made different proposals to diminish this complication. Suggestions like increasing the number of anchoring components,[146] using two stents with more than 3 cm of superposition,[140] modifying the proximal part of a partially covered stent with two threads of polypropylene that will be exteriorized and fixed,[147] or deploying an uncovered stent inside a covered stent have been proposed.[148] Slightly stiffer, less compliant and longer stents have also been suggested for reducing migration.[136]

On the other hand, stricture due to mucosal hypertrophy is a less common occurrence. No hyperplasic strictures were reported in our series. Incidence is not well described in literature and it is usually during the first two months after stent placement but also at a later stage.[149] Van Boeckel et al [38] in a systematic review found that tissue overgrowth was higher with PSEMS (12%) compared with SEPS (3%) and FSEMS (7%) (p = 0.68) although this result was not significant.

Moreover, tissue in- and/or overgrowth may complicate removal of PSEMS in patients, resulting in a second esophageal perforation.[150] Hirdes et al [151] describe a technique to remove embedded PSEMS placing a fully covered stent of the same diameter inside the FSEMS. This so-called stent-in-stent method causes necrosis of the hyperplasic tissue. In their experience, both stents can be removed uneventfully after a period of 7–14 days.

Complication rate of SEMS versus reoperation is lower and reduces healing time, hence recovery time, morbi-mortality rates and avoids other aggressive and expensive procedures.[20,45,48,61,123,125,130,140] Successful stent removal after leak sealing was 75% in our study. Among reasons for failed endoscopic extraction are stent migration and mucosal hypertrophy. In our study 2 cases (25%) of migration were reported, only 1 underwent surgery for stent extraction; migration rate in literature is 22.5% (range 9-53). Our intrahospitalary mortality rate due to endoscopic procedures was 0 while in the literature review mean was 7% (ranges 2-50%). It may well compare favorably with mortality rate after surgical management, 6.6% in our series.

It is to be noted that other mini-invasive endoscopical treatments, such as clips, fibrin sealants (FS) and vicryl plugs, were used providing leak sealing in 33.3% of the cases. FS have been widely used in surgery and there is a long experience. Literature confirms its efficacy, demonstrates local tolerance and the absence of undesirable effects and contraindications but very little is published about the use of FS in early treatment of GJ leaks. Small wall defects would specially benefit from them.[152–155]

Nowadays the use of FS is reported in cases or small series.[32,152,156] Brolin et al [54] reported 3 patients with IAAL after LGBP who received FS, 2 of these closed after one treatment only. The mean length of stay was 33 days. This group concluded that FS provides safe and successful treatment of patients who develop gastric leaks after bariatric operations. Böhm et al [156] have proposed a treatment algorithm combining FS and vycril mesh. They reported 39 cases of anastomotic leaks after surgery for UGI cancers that were treated with FS alone (n=24) or with combination of Vicryl plug and FS (n=15), showing complete healing after one to four sessions in 13 of the 15 patients (87%) who underwent

vycril/FS treatment. There is also an anecdotic case report of n-butil-2-cyanocrylate (Hystoacryl®) via submucosal injection into the lateral walls of the fistula rather than injection into the fistula.[157] The glue is injected into the submucosa until the lumen is occluded, ensuring that the fibrin plug does not become dislodged. No abrasion or depithelialization of the fistula tract is required. Also Kumar et al [158] have recently published novel endoscopic therapies that have demonstrated safety, such as a mushroom shaped metallic stent, nitinol clips or a vacuum assisted sponge closure (VAC) therapy. They conclude that these devices are steadily building evidence for efficacy relative to surgical management.

In conclusion, protocols for endoscopic treatment (retrieval, replacement, association of a concomitant treatment) are needed, as well as randomized trials to compare different stent types and the ideal stent design. However, due to the limited number of patients, this is unlikely to occur.[38] Research is conducted to biodegradable formulations to cover ruptures or anastomotic leaks.[38] This material has been shown to stimulate connective tissue and vascular ingrowths and displays only minor hyperplasic tissue formation.[159]

4.4. PREVENTION

Multiple preventive actions can be applied. As other authors, our team believes that these procedures should be performed in an experienced and accredited center after preoperatory selection and optimization of patients. Although there is no clear explanation for such a finding, this may be correlated with overall cardio-circulatory function and its influence on the blood supply and tissue oxygenation at the anastomotic site.[12] In oncologic resections, the nutritional status and cachexia of the patient are so important for success. In this cases, our group has experience placing, radio-guided or via endoscopy, a gastrostomy to ensure optimization of patient's nutrional status allowing the patient to be considered as a candidate for surgery.

On the other hand, patients with morbid obesity usually present with associated comorbidities at the time of evaluation and surgery. They are considered high-risk patients and should be evaluated thoroughly before their operation using a multidisciplinary team approach to select appropriate candidates.[13] In the late 1980s, LSG has been proposed as a step procedure in high-risk patients, followed

by a second step Roux-en-Y gastric bypass or biliopancreatic diversion and duodenal switch.[160,161] It must be noted in this context that the primary limiting factor in surgery in the super-obese is the volume of the left lobe of the liver: a greatly thickened left lobe diminishes and/or impedes visualization of the GEJ and His angle. In our center, patients with BMI >45 kg/m^2 and/or hepatomegalia are submitted to a high-protein, low-carbohydrate diet one week before surgery in order to reduce hepatic fatty infiltration and size of left hepatic lobe.[162] For this same reason Nguyen et al [163] had proposed a staged Roux-en-Y procedure with a low GJA and a larger gastric pouch. The low anastomosis obviates the need for exposure of the GEJ and His angle. At the second stage procedure, completion sleeve gastrectomy of the gastric fundus is performed at an interval of 6-12 months after the first stage operation.

Regarding the association of anastomotic leak rate and the experience of surgeon, Migita et al [10] state in their series that the experience of the surgeon was not a significant variable relating to the incidence of the anastomotic trouble, nor the development of EJAL. They suggest that skills of surgical teams, rather than individual surgeons, are important when considering surgical quality. Our group believes that the contributions by industry have been also a decisive factor. The development of a triple-staple line device (Echelon ®) which applies the same pressure along the length of the cartridge making possible that staple formation is the same in the beginning and in the end *(figure 32)*, has been crucial.

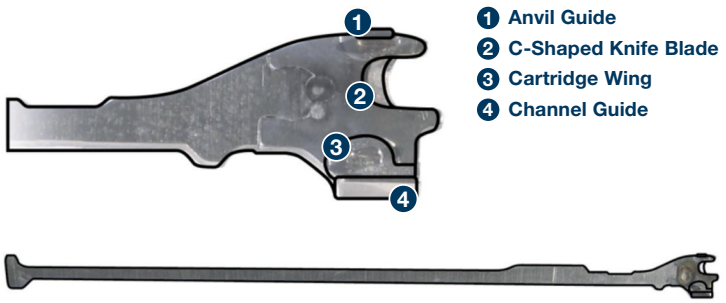

Figure 32: Parts of a laparoscopic stapler device.

Baker et al [33] evaluated and reviewed different ways to optimize the staple-line strength concluding that under-sizing staple cartridge increases the risk for inadequate staple formation or can lead to

excessive tissue compression leading to tearing and perforation. They establish that staples of 4.8mm should be used on thick stomach because they are designed to be stronger and form longer leg lengths. They also suggest that great care must be used in firing the endocutters, avoiding a bunch of tissue at the crotch of the stapler. The group insists that surgeon must watch and remove the "migratory crotch staple" *(figure 33)*. In their study full-thickness over-sewing past a fixed staple-line *(figure 34)* is not recommended because it may increase the risk of tearing at the point of suture penetration in a distended gastric pouch. This effect is not likely to be significant in low-pressure areas.

Figure 33: Migratory crotch staple. [33]

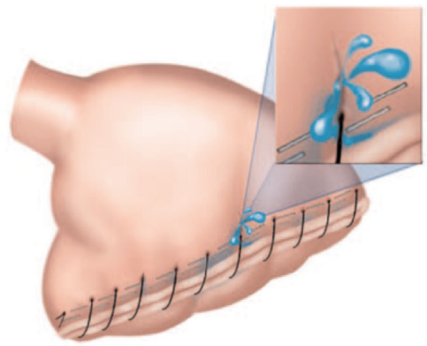

Figure 34 : Oversewing causing leaks when the pouch is distended and suture bowstrings and tears tissue. [33]

Moreover, the recent outbreak of unidirectional barbed sutures has been proposed to simplify wall and mesentery closure in laparoscopy.[67,164–166] Our center has recently published two studies: one with the largest series for GJA in LGBP [67] and the first study to describe this suture in laparoscopic gastro-intestinal anastomoses.[166] Among them, 177 laparoscopic GJA (172 during Roux-en-Y GBP and 5 after gastrectomy), 5 EJA, and 22 JJA (4 after small bowel resection and 18 during GBP or gastrectomy) were required. Senior and training surgeons performed them. There was no conversion to usual sutures. One fistula occurred in an EJA and was managed conservatively. One self-limited anastomotic bleeding occurred, and no anastomotic stenosis occurred during 6 months of follow-up evaluation. As conclusion, barbed sutures for laparoscopic intestinal anastomosis are safe and reproducible. Therefore barbed sutures have been incorporated systematically in our surgical technique for intestinal anastomosis simplifying one of the most complex and time-consuming procedures. The use of this thread should not be considered as offsetting the inexperience of the surgeon in laparoscopic suturing, but to improve it in an area where exposure and continuous traction are often difficult.[167]

Therefore performing an EJA with barbed suture is simplified. There is no standardized technique for re-establishment of gastrointestinal continuity after total gastrectomy.[166] Bracale et al [82] concluded that a laparoscopic intracorporeal side-to-side EJA is a safe and feasible technique. It represents a valid method for performing a reconstruction of the digestive tract in laparoscopic surgery after LTG, especially in presence of a narrow esophagus. Our group has also published our technique for the manual creation of a feasible, safe, tension-free and effective EJA *(figure 35)*. Any surgeon familiar with laparoscopic surgery and the principles of oncological resection can perform it. The cost is also relatively low because neither a circular stapler nor other special equipment is required.[66,67,166,167]

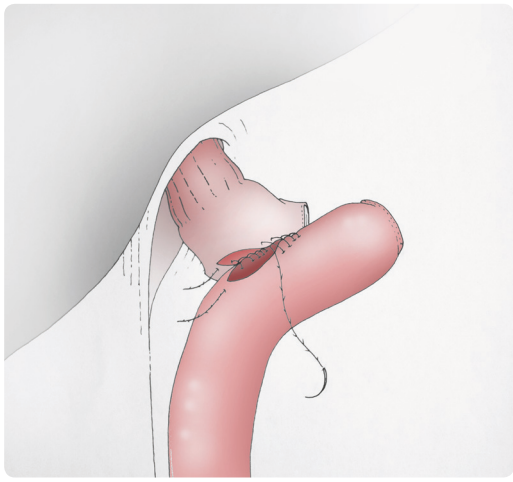

Figure 35 : 95% gastrectomy is performed to reduce comorbities associated to esophago-jejunal anastomosis.

To reduce as much as possible morbid-mortality in EJA for cancer gastric surgery, the recent tendency is to take into consideration in selected cases (proximal tumors, poorly differentiated diffuse tumors) the near total or 95% oncologic gastrectomy (G95%). Described by japanese authors [168,169] in early 80s, actually it has been reconsidered by a laparoscopic approach with promising results.[170–172] Our laparoscopic technique *(figure 36)* has been published not long ago.[170] It consists on leaving a little gastric pouch 2cm long which permits performing a GJA rather than EJA, expecting to reduce leak rate while, at the same time, proximal oncologic resection margins are respected. Compared to 7/8 gastrectomy, G95% allows a complete resection of the fundus and lymphadenectomy of stations 1 and 2. This technique achieves good short-term outcomes and good quality of life respecting latest oncological criteria about proximal resection margin resection.[167,170,173]

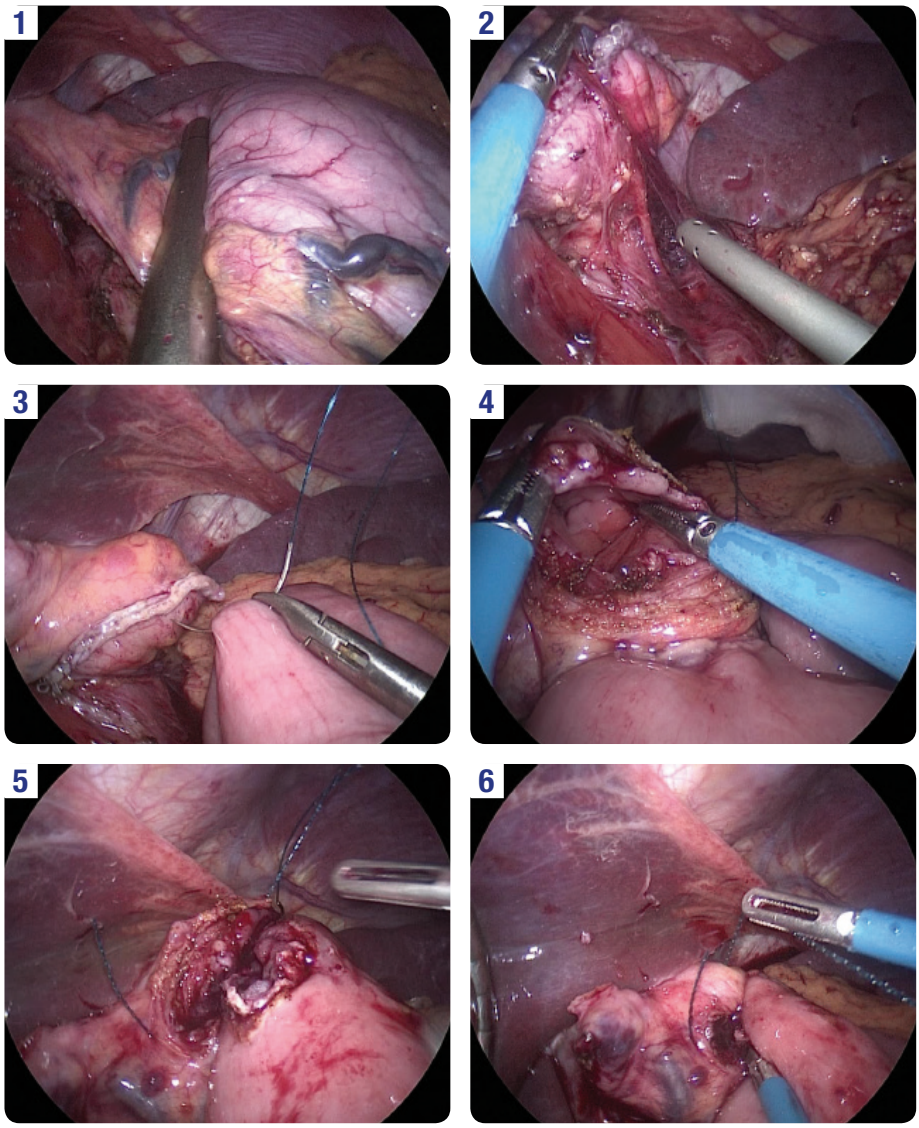

Figure 36: Gastrectomy 95% and steps to make gastro-jejunal anastomosis.
1: Gastric section. **2**: Identification and preservation of posterior gastro-phrenic artery **3**: Gastro-jejunal anastomosis: posterior layer. **4**: Verifying previous step. **5**: Reinforcement of posterior layer. **6**: Gastro-jejunal anastomosis: anterior layer.

As regards bariatric surgery, having a thorough knowledge of anatomy of His angle, performing a careful dissection of this area and avoiding strictures by diverting slightly to the left in the last shot [16,160] are important technical considerations that surgeon must take on account in order to prevent leaks. Kravetz et al [174] compared in a retrospective study manual versus mechanical anastomosis in LGBP. No difference was appreciated in the anastomotic leak or re-exploration rate with either technique.

However, the incidence of anastomotic stricture in their series tended to be lower with a hand-sewn technique with lower operative time.

About reinforcement of staple line in LSG (with suture or Gore® Seamguard®) Dapri et al [175] compared between no staple line reinforcement, buttressing of the staple line with Gore® Seamguard® and staple line suturing in a prospective and randomized study (n=75). They concluded that no significant difference was evidenced in terms of postoperative leak between the three techniques of LSG and Gore® Seamguard® statistically reduces blood loss during stomach sectioning as well as overall blood loss. In the other side, Choi et al [176] in a meta-analysis shows that reinforcing staple-line decreases incidence of postoperative leak and overall complications. Nevertheless, like other authors [177,178] Choi et al, note that more prospective studies with better evidence are needed. Our experience with our standardized technique is that no staple line reinforcement is safe and effective, with the exception of evidence of active bleeding of the staple-line during surgery. In this case, we opt for reinforcement with barbed suture.

In relation to the use of fibrin sealants in the prevention of GJAL nowadays there is no clear evidence supporting this use.[59,121]

Intraoperative leak assessment using endoscopy and/or distension of the anastomosis with dye, air or other gas might be useful to detect leaks that can be repaired during the procedure. Nishikawa et al [179] propose an intra-operative endoscopy after total gastrectomy as a safe and feasible method that can accurate significant information to reduce post-operatory leak detecting the default in EJ anastomosis. To achieve it, anastomosis is submerged in saline solution, alimentary limb is clamped and air is insufflated through the endoscope. Presence or air bubbles around the anastomosis point out the possibility of a leak.[180] The last ASMBS guideline concluded that these techniques have not been shown to decrease the risk of leak after surgery.[121]

Another controversial point is placement of prophylactic drains.[2] Although some surgeons have advocated routine placement of drains in proximity to the anastomosis to better diagnose and/or control

leakage others have supported that they are unnecessary and might increase the risk of a leak developing.[121] Therefore we place them routinely after cancer surgery and selectively after benign surgery.

To conclude this point, it is worth mentioning the study by Haga et al [181] where a prediction scoring system of anastomotic leak, "Estimation of Physiologic Ability and Surgical Stress" (E-PASS), is analyzed prospectively. It concludes that, requiring only nine variables, this method may be useful in predicting anastomotic leak and its prognosis in various kinds of gastrointestinal surgical procedures. The disadvantage is that this formula is not easily applicable in the bedside of the patient given that 9 variables have to be collected (age, presence of severe heart disease, severe pulmonary disease, diabetes, performance status scale, ASA score, blood loss related to weight, operative time, length of cutaneous incision).

4.5. LIMITATIONS OF THE STUDY

This study has several limitations. First the small number of patients with IAAL included in this study is small, but when referred to the number of patients who underwent UGI surgery in our center, we think that results must be, al least, considered. Therefore, the level of evidence extracted from our study is not as strong as the level of evidence from prospective, randomized, controlled trials; however, due to the limited number of patients, this is unlikely to occur, since to detect a 10% reduction in hospital stay, for example, thousands of patients per arm would be needed.

Second, given the retrospective nature of our study, the potential for selection bias is a possibility. In addition, a variety of surgical techniques of performing anastomosis have been employed in the included studies. In some patients, anastomosis was done in another center, in other cases different devices and sutures were used, such as barbed sutures or current sutures or double staple line cartridges. Consequently, this could have affected clinical success rate, but also complication and mortality rates.

Finally, selection bias cannot be excluded in this patient group, as it has still not been elucidated which patients could benefit from stenting and which patients from primary surgery. Further randomized trials are, however, needed to compare different stent types, on one hand, and the ideal stent design that comes out of these trials with surgical treatment, on the other hand.

4.6. MANAGEMENT ALGORITHM

To conclude, I would like to propose an algorithm for the management of IAAL after UGI surgery *(figure. 37)*.

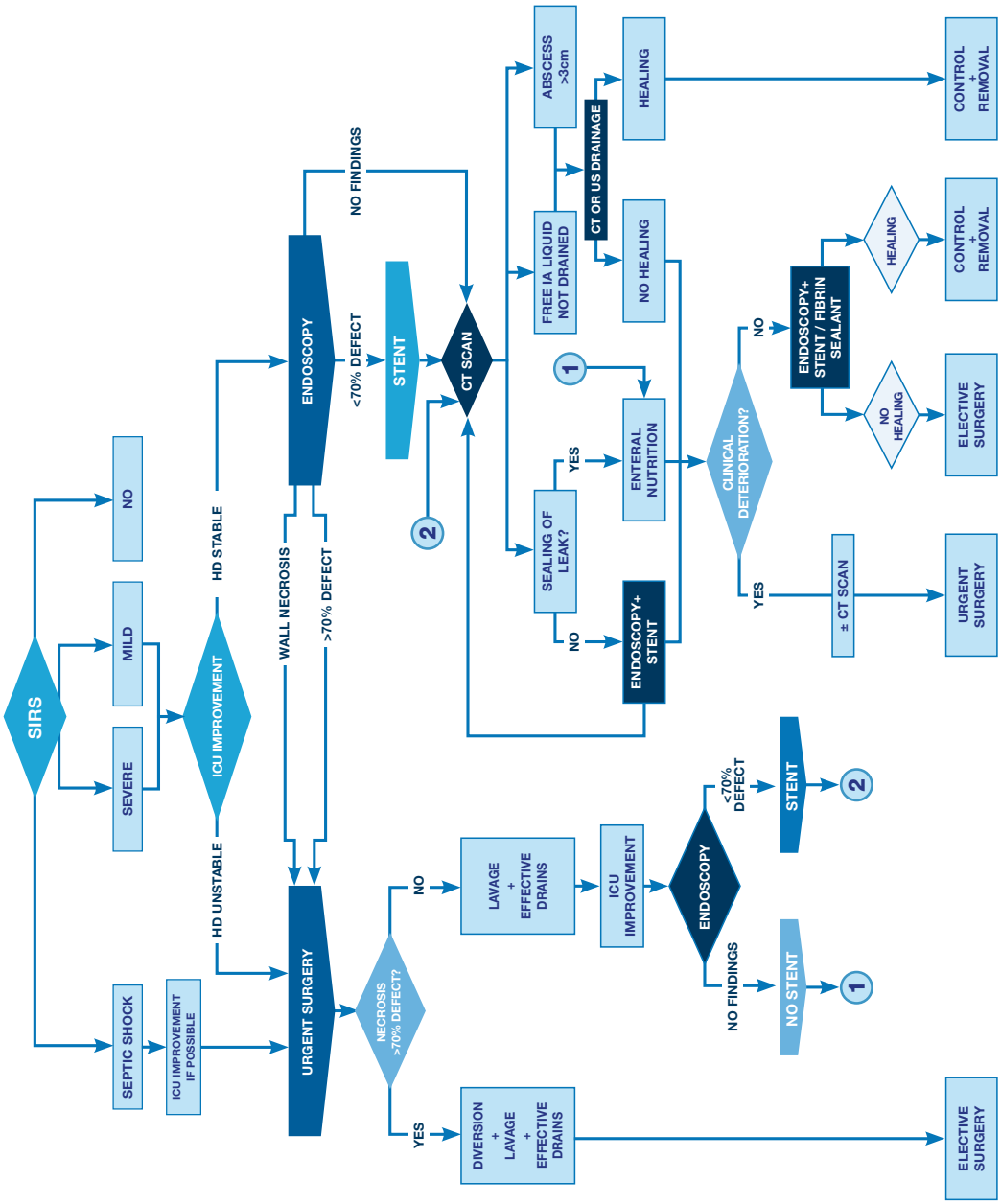

Figure 37 : Flowchart proposed for the managment of IAAL.

conclusions

Conclusions

1. Although there is a downward trend, intraabdominal anastomotic leak after upper gastrointestinal surgery is a serious complication: efforts must be made to decrease its incidence in order to diminish morbi-mortality and the high economic cost to society.

2. A universally accepted definition of intraabdominal anastomotic leakage after upper gastrointestinal surgery is needed, as well as common agreed standardized diagnostic algorithms and uniform grading of severity. This may contribute to have uniform criteria that would facilitate valid comparison of the results of different studies improving its management.

3. Prevention is our most important asset: patient selection by a multidisciplinary team, adequate surgery indication, preoperatory optimization and a standardized surgical technique.

4. Early diagnosis of intraabdominal anastomotic leak is paramount: it cannot be based on clinical suspicion alone. Therefore an endoscopic exploration should be performed when possible allowing early diagnosis, providing information of anastomosis' morphologic characteristics to help accurate the best management. Eventually, treatment can be done at the same time.

5. Multidisciplinary treatment combining endoscopical, surgical (laparoscopic) and radiological techniques is the best strategy to reduce time until leak healing. It must be achieved in a specialized center: adequate drainage of the abdominal collection, nutritional support and a rigorous clinical and radiological follow-up are essential.

6. In hemodynamic stable patients, conservative management can be effective and can obviate a reintervention, thereby avoiding postoperative complications.

7. Surgical management is the definitive treatment in hemodynamic unstable patients. Laparoscopic approach allows evaluation of anastomosis' characteristics, consents a peritoneal lavage and positioning effective drains. Laparotomy remains anecdotal for hemodynamic unstable non-responding patients excluded of mini-invasive treatment.

8. Endoscopical treatment with temporary stent placement and removal with low procedure-related morbidity and mortality is feasible and can be a definitive treatment in adequately perfused upper gastrointestinal surgery anastomotic leakage. Because of the favorable outcome of stent therapy compared with other treatment regimens, we can suggest stent therapy as the treatment of choice in this situation.

9. Temporary stent can help cronify a leak until a definitive surgery can be performed in an optimal clinical and nutritional status of the patient.

10. However, because stent migration remains a common problem in postoperative patients, the optimal type of stent, the best time for stent removal, and useful additional endoscopic means for stent fixation have yet to be defined in these patients.

Conclusiones

1. A pesar de que hay una tendencia decreciente, la IAAL tras la cirugía supramesocólica es una complicación seria: se deben dirigir los esfuerzos a disminuir su incidencia y así rebajar la morbi-mortalidad y el alto coste económico que ello supone a la sociedad.

2. Es necesario una definición universalmente aceptada de dehiscencia anastomótica intraabdominal tras cirugía supramesocólica, así como algoritmos de diagnóstico comunes, acordados y estandarizados y un sistema de clasificación de severidad uniforme. Ello puede contribuir a tener un criterio equiparable que facilite una comparación válida de resultados entre diferentes estudios, mejorando de este modo su manejo.

3. La prevención es la mejor herramienta: la selección de paciente por un equipo multidisciplinar, una adecuada indicación quirúrgica, la optimización preoperatoria y una técnica quirúrgica estandarizada.

4. El diagnóstico precoz es sumamente importante: no puede basarse tan solo en la sospecha clínica. Por eso se debería realizar un exploración endoscópica que permita el diagnóstico temprano, al mismo tiempo que da información de las características morfológicas de la anastomosis que permitirá el manejo más adecuado.

5. El tratamiento multidisciplinar combinando técnicas endoscópicas, quirúrgicas y radiológicas es la mejor estrategia para reducir el tiempo hasta el sellado. Debe de llevarse a cabo en centros especializados siendo esenciales un drenaje adecuado de la colección intraabdominal, soporte nutricional y un seguimiento estrecho clínico-radiológico.

6. En pacientes con estabilidad hemodinámica el manejo conservador puede ser efectivo y evitar la reintervención y evitando por lo tanto las complicaciones postoperatorias.

7. El manejo quirúrgico es el tratamiento definitivo en pacientes con inestabilidad hemodinámica. El abordaje laparoscópico consiente la evaluación de las características de la anastomosis, permite el lavado de la cavidad peritoneal y la colocación de drenajes efectivos. La laparotomía

se limita a casos anecdóticos, pacientes inestables no respondedores excluidos del tratamiento mini-invasivo.

8. El tratamiento endoscópico de un stent temporal y su retirada, teniendo este procedimiento una baja morbi-mortalidad, hace que sea factible y que pueda ser el tratamiento definitivo en IAAL con una buena perfusión. Debido al resultado favorable del tratamiento con stent frente a otros tratamientos, podemos sugerir el stent como tratamiento de elección en esta situación.

9. Un stent temporal puede cronificar la dehiscencia hasta poder instaurar un tratamiento quirúrgico definitivo cuando las condiciones clínicas y nutricionales del paciente lo permitan.

disclosures

Disclosures

The author claims no commercial associations that might be a conflict of interest in relation to this study.

This study has been accepted in:

- 3rd International Congress of the EAES. Bucharest 3-6 June 2015
- XIII Reunión Nacional de la Sección de Cirugía Endoscopica de la AEC. Alicante, 13-15 May 2015

By the time this study is being printed, I am waiting for acceptance in:

- XX Reunión Nacional de la Asociación Española de Cirujanos. Granada 21-23 October 2015

appendix

Appendix A - Classification of surgical complications Clavien-Dindo [63]

Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs (antiemetics, antipyretics, analgesics, diuretics, electrolytes, physiotherapy). This grade also includes wound infections opened at the bedside.
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are included.
III	Requiring surgical, endoscopic or radiological intervention.
IIIa	Interventions not under general anesthesia.
IIIb	Interventions under general anesthesia.
IV	Life-threatening complication (including CNS complications) requiring IC/ICU management.
IVa	Single organ dysfunction (including dialysis).
IVb	Multiorganic dysfunction.
V	Death of a patient.

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